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CLXVII.—*A New Scaly Variety of Aluminium Hydroxide.*

By Panchanan Neogi and Anil Krishna Mitra.

Although several varieties of aluminium hydroxide have been described, there is no definite evidence that any of them are crystalline. The gelatinous precipitate obtained by adding ammonia to solutions of aluminium salts was stated by Ramsay (J., 1877, **32**, 395) to be $Al_2O_3,5H_2O$ if air-dried, or Al_2O_3,H_2O if dried at 300° but Allen (*Chem. News*, 1900, **82**, 75) found that the amorphous hydrate had the composition $Al_2O_3,3H_2O$ and was converted into $Al_2O_3,2H_2O$ if heated at 100° or dried over sulphuric acid. Tommasi (*Chem. Zentr.*, 1905, ii, 605) described what he called a δ-modification ($Al_2O_3,3H_2O$), obtained by keeping the ordinary hydroxide under water for several months; this was amorphous and dissolved in acids and alkalis with difficulty. A so-called β-modification (also $Al_2O_3,3H_2O$) has been described by Noyes and Whitney (*Z. physikal. Chem.*, 1894, **15**, 694) and others as being deposited from soluble aluminates; this was regarded as identical with the crystalline mineral gibbsite (Ditte, *Compt. rend.*, 1893, **116**, 183) until Russ (*Z. anorg. Chem.*, 1904, **41**, 216) showed that it was not crystalline.

Whilst reducing various nitrates by means of the aluminium–mercury couple, we met with glistening scales which were shown by careful qualitative tests to be pure aluminium hydroxide. These are stable and have the composition $Al_2O_3,4H_2O$ and $d^{31°}$ 1·5490. Under the microscope, they show reflexions from innumerable planes, but no doubly-refracting crystals and no resemblance to gibbsite; in view of the flaky appearance, however, it is probable that the substance consists of isometric crystals. As recrystallisation was impossible, no crystals have been obtained large enough to permit of crystallographic classification.

By the action of the aluminium–mercury couple in water alone, aluminium hydroxide is obtained in a gelatinous condition mixed with black particles (Reichard, *Pharm. Z.*, 1907, **40**, 569), so that it is not justifiable to assign a definite composition to it (compare Cossa, *Z. Chem.*, 1879, **13**, 443).

Certain other nitrates and nitrites, such as those of the alkali metals, give a scaly aluminium hydroxide under the same conditions, but it is often accompanied by a much larger quantity of the gelatinous variety, and barium (and, to a less extent, strontium) nitrate gives the best product.

Besides the nitrates, aqueous solutions of the alkali bromates and iodates were similarly reduced, and the aluminium hydroxide

obtained again consisted of a mixture of the gelatinous and scaly varieties, but was usually contaminated with halides.

Experimental.

The freshly-prepared aluminium–mercury couple was added to a concentrated solution of barium nitrate, which covered it to a depth of one or two inches. The reaction commenced at once with the evolution of heat, and the flask was then closed with a soda-lime tube to exclude carbon dioxide and immersed in ice-water. Bright scales of aluminium hydroxide were deposited on the couple, and after a few minutes the supernatant liquid together with the hydroxide was transferred to a large conical flask, which was closed with a cork in order to prevent access of atmospheric carbon dioxide. The couple could be used again with fresh solution and the supernatant liquid in the large flask could be decanted and used again. A quantity of the scales was thus obtained in a few hours; they were repeatedly washed by decantation with large volumes of water until free from barium and any gelatinous variety accompanying it, filtered off, and washed with alcohol and finally with ether. They dried rapidly, retained their lustre in a desiccator, and showed no tendency to absorb water during preparation for analysis, as is the case with the ordinary amorphous variety.

The scales were dissolved in hydrochloric acid and tested for mercury with negative results. (Hasty or negligent washing without repeated decantation leaves traces of barium and mercury.) They were also found to be free from nitrate, nitrite, nitrogen, and peroxidic oxygen.

Ignition of the substance, dried for several days, in a platinum crucible showed a loss of 41·0, 41·2% (Calc. for $Al_2O_3,4H_2O$: 41·4%). Strong ignition in a current of dried air yielded 41·6, 41·0% to calcium chloride tubes, the last molecule of water being removed only with difficulty. Aluminium was estimated after solution in hydrochloric acid (Al_2O_3, found : 59·05, 58·85. Calc. : 58·6%). Loss at 100°, 11·1 (Calc. for $1H_2O$: 9·6%). After the substance had been kept for 3 weeks in a desiccator, its composition, $Al_2O_3,4H_2O$, was unchanged.

The scales were soluble in mineral acids, but insoluble in methylamine, in which the ordinary precipitated hydroxide is soluble (Renz, *Ber.*, 1903, **36**, 2751).

We offer our thanks to Professor S. L. Biswas of the Geological Department of this College for kind assistance in the microscopic examination.

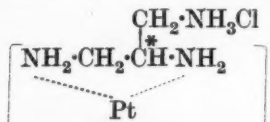
Presidency College, Calcutta. [*Received, August 30th,* 1926.]

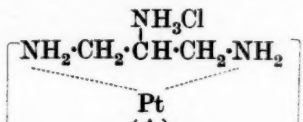
CLXVIII.—*Tetrachloro(triaminopropane-γ-monohydrochloride)platinum, an Optically Active Complex Salt of a New Type.*

By FREDERICK GEORGE MANN.

IT has recently been shown by the present author (J., 1926, 2681) that αβγ-triaminopropane, $NH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2$, co-ordinates with platinum and copper to give two complex salts of novel type, in which only two of the three amino-groups in the triaminopropane molecule are joined to the metal, the third being free for normal salt formation with acids. Quadrivalent platinum thus gives tetrachloro(triaminopropane-monohydrochloride)platinum, $Cl_4Pt,NH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2,HCl$ (I). Here the metallic complex consists of platinum, of co-ordination number 6, linked to four chlorine atoms and to two of the three amino-groups of the base: it is therefore neutral and non-ionic, being, in its co-ordination linkages, of the same general type as tetrachloroethylenediamine-platinum, $[Cl_4PtNH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2]$. Since, however, the third free amino-group, being unco-ordinated and outside the ring, forms a hydrochloride, the compound in solution furnishes one chlorine ion.

Such a compound may exist in two alternative forms. The platinum may either be co-ordinated to the α- and β-amino-groups, leaving the γ-amino-group free to form the monohydrochloride (II), in which case the triamine is acting for co-ordination purposes as a substituted ethylenediamine, or, alternatively, the platinum may be co-ordinated to the α- and γ-amino-groups, leaving the β-amino-group free to form the hydrochloride (III); in this case the triamine is acting as a substituted trimethylenediamine. A possible method of deciding between these two alternative constitutions was at once suggested by the fact that co-ordination through the α- and β-amino-groups (II) causes the carbon atom marked * to become asymmetric, since it is linked on the one hand to a methylene-amino-group (·$NH_2{\cdot}CH_2$·) and on the other to a methylene-ammonium radical (·$CH_2{\cdot}NH_3$·). Such a compound should therefore be capable of resolution into optically active forms.

(II.) 



(III.)

Co-ordination through the αγ-diamino-groups (III) gives, however, a symmetrical compound which cannot be so resolved

Attempts were therefore made to resolve this compound by converting the hydrochloride of the free amino-group into the corresponding *d*-camphor-β-sulphonate. The latter compound on fractional recrystallisation from water gave finally l-*tetrachloro*-(*triaminopropane-mono*-d-*camphor*-β-*sulphonate*)*platinum*, having $[M]_{5461}^{15°} = -426°$. This compound on treatment with calcium chloride gave the l-*tetrachloro*(*triaminopropane-monohydrochloride*)-*platinum* of $[M]_{5461}^{15°} = -502°$. The racemic product was then converted into the *l*-camphor-β-sulphonate, which on recrystallisation furnished similarly d-*tetrachloro*(*triaminopropane-mono*-l-*camphor*-β-*sulphonate*)*platinum*, having $[M]_{5461}^{15°} = +424°$, which was in turn converted into the d-*tetrachloro*(*triaminopropane-monohydrochloride*)*platinum* of $[M]_{5461}^{15°} = +501°$. The two optically active monohydrochlorides differ further from the racemic compound in that they crystallise in the anhydrous form, whilst the racemic compound has one molecule of water, which is not readily removed (Mann, *loc. cit.*).

It follows from these results that the platinum compound has the constitution (II), *i.e.*, that the triaminopropane co-ordinates with platinum more readily through the α- and β-amino-groups to form a five-membered ring compound having an asymmetric element, than through the α- and γ-amino-groups, whereby a six-membered ring compound of high symmetry would have been formed.

It should be emphasised that not only is this platinum compound of entirely novel type, but the cause of its optical activity also is novel. All optically active complex salts hitherto recorded have owed their activity to one (or both) of two factors. Either the complex itself has been dissymmetric, and therefore capable of resolution, *e.g.*, the trisethylenediaminecobaltic complex,

$$[Co(NH_2\cdot CH_2\cdot CH_2\cdot NH_2)_3]'''$$

or, alternatively, the complex has contained a constituent dissymmetric molecule which has been resolved before the preparation of the complex salt. Thus *d*-αβ-propylenediamine,

$$NH_2\cdot CH_2\cdot \overset{*}{C}H(NH_2)\cdot CH_3,$$

gives a *d*-trispropylenediaminecobaltic complex,

$$[Co\{NH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_3\}_3]''',$$

the activity of which is due to the active nature of the constituent amine molecules: here, however, the complex also is itself dissymmetric, and a secondary activity can be manifested by the complex as a whole. In the platinum compound under discussion, however, asymmetry of the central (or β) carbon atom is induced by the mode of co-ordination of the triaminopropane molecule and by the consequent orientation of the co-ordination linkages: the asymmetry of this element therefore does not arise until the co-

ordination compound itself is formed. This is the first case to be recorded in which the asymmetry of a carbon atom arises from the operation of auxiliary valencies.

Attempts have been made to replace the four co-ordinated chlorine atoms in tetrachloro(triaminopropane-monohydrochloride)-platinum with further basic groups by treating the compound in solution with ammonia and with ethylenediamine. The action of such bases is, however, solely to withdraw the hydrogen chloride from the free amino-group: the latter at once co-ordinates with the platinum, expelling a chlorine atom from the complex, and the insoluble *trichlorotriaminopropaneplatinic monochloride*,

$$[Cl_3PtNH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2]Cl,$$

is thus formed.

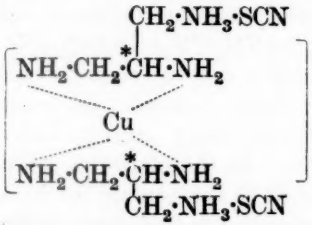
Tetrachloro(triaminopropane-monohydrochloride)platinum gives a characteristic reaction when treated in solution with oxalic acid, since the very slightly soluble *tetrachloro(triaminopropane-hydrogen-oxalate)platinum*, $[Cl_4PtNH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2,(CO_2H)_2]$, is rapidly precipitated. When this compound is boiled for several hours in aqueous solution, both the unco-ordinated amino-group and the oxalic acid enter the complex, displacing three chlorine atoms, thus furnishing *monochloromonoxalatotriaminopropaneplatinic monochloride*, $[Cl(CO\cdot O\cdot)_2PtNH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2]Cl$.

It has also been shown (Mann, *loc. cit.*) that copper co-ordinates with triaminopropane to give salts such as *bis(triaminopropane-monothiocyanate)cupric dithiocyanate*,

$$[Cu\{NH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_3(SCN)\}_2](SCN)_2 \quad (IV).$$

Here the copper atom is linked to two molecules of the base, but, since it has a co-ordination number of 4, to only two amino-groups in each molecule of the triamine. The metal is thus fully co-ordinated, and the complex therefore bivalent; the two unco-ordinated amino-groups, however, as in the platinum compound, are neutralised by normal salt formation, and in solution thus furnish two additional ions. It would follow by analogy that the αβ-diamino-linkage probably obtains also in this copper compound, which

(V.)



would then have the constitution (V), the carbon atoms marked * being asymmetric. Such a compound should exist in racemic,

dextro-, lævo-, and *meso*-forms, and if the four co-ordination linkages of the copper are directed to the corners of a regular tetrahedron (Mills and Gotts, J., 1926, 3121), the dextro-, lævo-, and *meso*-forms should each exist in two forms, in which the copper has the *d*- and the *l*-configuration respectively. In view of the intensely deep violet colour of these copper compounds, no attempts at resolution have yet been made.

Further work is now being carried out to determine the mode of co-ordination of triaminopropane with various noble metals, such as iridium and palladium, and with certain bivalent metals such as zinc, cadmium, and mercury, and to determine further whether such compounds are capable of resolution into optically active forms.

The various types of complex salts furnished by triaminopropane may be conveniently summarised here (Mann and Pope, *Proc. Roy. Soc.*, 1925, *A*, **107**, 80; J., 1926, 2675; Mann, J., 1926, 2682) :—

1. Metals of co-ordination number 4 :

A. Triaminopropane acting as a diamine : Bis(triaminopropane-γ-monothiocyanate)cupric dithiocyanate,

$$[Cu\{NH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_3\cdot SCN\}_2](SCN)_2.$$

B. Triaminopropane acting as a triamine : Tetratriaminopropane-tricupric hexathiocyanate,

$$Cu_3\{(NH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2)_4\}(SCN)_6.$$

2. Metals of co-ordination number 6 :

A. Triaminopropane acting as a diamine : Tetrachloro(triaminopropane-γ-monohydrochloride)platinum,

$$[Cl_4PtNH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_3Cl].$$

B. Triaminopropane acting as a triamine : (*a*) Triacido-triammine type. Trichlorotriaminopropaneplatinic monochloride,

$$[Cl_3PtNH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2]Cl.$$ (*b*) Hexammine type. Bistriaminopropanecobaltic trichloride,

$$[Co\{NH_2\cdot CH_2\cdot CH(NH_2)\cdot CH_2\cdot NH_2\}_2]Cl_3,$$

and the corresponding nickel and rhodium salts.

Experimental.

All rotations given in this paper have been measured at 15° in a 4-dcm. polarimeter tube, and, unless otherwise stated, are for the mercury green line ($\lambda = 5461$).

Preparation of Tetrachloro(triaminopropane-monohydrochloride)-platinum Monohydrate.—The following quantitative directions supplement the general directions already given (Mann, *loc. cit.*, p. 2686). A solution of triaminopropane trihydrochloride monohydrate (22 g.) in water (200 c.c.) is added to 100 c.c. of a solution

of chloroplatinic acid containing 10% of metallic platinum. The clear mixture is boiled under reflux for 3 hours, and the pale yellow solution so obtained twice evaporated to small bulk on the water-bath with intermediate addition of water. The solution is finally concentrated until crystals appear, and on cooling, tetrachloro-(triaminopropane-monohydrochloride)platinum monohydrate rapidly separates (20·3 g.). This material, after two recrystallisations from water, is pure, and darkens at 255—260° and melts at 272—273° (decomp.).

l-*Tetrachloro*(*triaminopropane-mono*-d-*camphor*-β-*sulphonate*)*platinum Semihydrate*,

$[Cl_4PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2,C_{10}H_{15}O{\cdot}SO_3H],\frac{1}{2}H_2O$.—Hot aqueous solutions of tetrachloro(triaminopropane-monohydrochloride)platinum monohydrate (20 g.) and silver *d*-camphor-β-sulphonate (10·4 g.) were mixed, boiled for 5 minutes, and filtered. The filtrate was evaporated to small bulk on the water-bath, fine, crystalline scales steadily separating; finally the product formed a semi-solid mush, which was at once chilled and filtered. The solid product so obtained was then recrystallised repeatedly from hot water to separate the *l*-base *d*-sulphonate from the more soluble *d*-base *d*-sulphonate. Recrystallisation was best carried out by drying each fraction thoroughly in a vacuum over sulphuric acid, and then adding the powdered product quickly with stirring to a small quantity of almost boiling water. A clear solution was thus rapidly obtained, and on filtering and cooling gave an ample crop of the sulphonate. The latter always retained half a molecule of water of crystallisation even after long exposure to sulphuric acid in a vacuum. After six recrystallisations from water, the *l*-base *d*-sulphonate was obtained as a pale lemon-yellow powder, which in 1·349% aqueous solution had $\alpha = -3{\cdot}44°$, whence $[\alpha] = -63{\cdot}7°$ and $[M] = -426°$: it darkened at 260° and melted to a tar between 270° and 285° (Found: Pt, 29·3. $C_{26}H_{56}O_9N_6Cl_8S_2Pt_2$ requires Pt, 29·25%). This sulphonate does not readily undergo racemisation at the ordinary temperature, since cold aqueous solutions retained their activity unchanged for a week.

A dextrorotatory product also could be separated in the above experiments, for when the cold aqueous mother-liquor from the second fraction was diluted considerably with alcohol and kept over-night, a crop of the camphorsulphonate separated which, in 1·572% solution, had $\alpha = +3{\cdot}08°$, whence $[\alpha] = +49{\cdot}0°$ and $[M] = +323°$. This was thus evidently an optically impure *d*-base *d*-sulphonate, and attempts were made to purify it by repeated dissolution in water and reprecipitation with alcohol. These experiments did not, however, give satisfactory results, and

the optically pure dextro-salt was finally obtained by recrystallisation of the *l*-camphorsulphonate, as described below.

l-*Tetrachloro*(*triaminopropane-monohydrochloride*)*platinum*.—The sixth fraction of the *l*-tetrachloro(triaminopropane-mono-*d*-camphor-β-sulphonate)platinum, having $[M] = -426°$, was dissolved in a little hot water and the solution was chilled, filtered, and diluted with concentrated aqueous calcium chloride solution. After 4 hours the fine, crystalline monohydrochloride which had separated was collected, well washed with alcohol and ether, and dried. The pure anhydrous l-*monohydrochloride* thus obtained retained its original crystalline form during the processes of filtering and drying; it had evidently, therefore, separated originally in the anhydrous form, and not lost water of crystallisation whilst being dried. It darkened at 260—265° and melted at 277—278° (decomp.) (Found: Pt, 42·2. $C_3H_{12}N_3Cl_5Pt$ requires Pt, 42·2%). A 1·407% aqueous solution had $\alpha_{5780}^{15°} = -5·24°$, whence $[\alpha]_{5780}^{15°} = -93·1°$, $[M]_{578}^{15°} = -431°$, and $\alpha_{5461}^{15°} = -6·10°$, whence $[\alpha]_{5461}^{15°} = -108·4°$, $[M]_{5461}^{15°} = -502°$.

Certain observations made in the course of the above work point strongly to the fact that the resolution is successful only if the camphorsulphonate crystallises at a low temperature, and that at higher temperatures it is probably the racemate, or even a product containing an excess of the opposite enantiomorph, which separates. Thus, in the initial preparation, the first crop of crude *d*-camphorsulphonate was obtained by evaporating the solution on the water-bath and then filtering off the solid product which separated. Since the *l*-base *d*-sulphonate is less soluble (in cold water) than the *d*-base *d*-sulphonate, the filtrate from this first crude product should have contained an excess of the *d*-base *d*-sulphonate. Actually it contained an excess of the *l*-base, and when treated with calcium chloride gave a markedly lævorotatory hydrochloride which, in 1·672% aqueous solution, had $\alpha = -0·78°$, whence $[\alpha] = -11·7°$. When the first crop of crude *d*-camphorsulphonate was subjected to its first recrystallisation, the second fraction obtained now separated after the solution had been chilled; it possessed, of course, an increased lævorotation, and the mother-liquor now contained an excess of the *d*-base, and when treated with calcium chloride gave a feebly dextrorotatory hydrochloride. All the successive fractions also separated after their solutions had been chilled, and the resolution thus proceeded smoothly to completion. It was further observed that if the initial filtrate from the first crop of crude *d*-camphorsulphonate was kept, in the course of 24 hours long, pale lemon-yellow needles of the almost optically pure *l*-base *d*-sulphonate separated, and after several days became contamin-

ated with orange-coloured prisms, presumably those of the *d*-base *d*-sulphonate. In some preparations of the *d*-camphorsulphonate, these long, pale lemon-yellow needles were filtered off before the separation of the orange prisms; they were washed with a little water, and placed over sulphuric acid in a vacuum; they then rapidly lost their crystalline form on partial dehydration, and gave the semihydrate of the almost optically pure *l*-base *d*-sulphonate. Two such samples gave the following rotations respectively: (*a*) a 1·008% aqueous solution had $\alpha = -2{\cdot}53°$, whence $[\alpha] = -62{\cdot}7°$ and $[M] = -419°$; (*b*) a 1·184% solution had $\alpha = -2{\cdot}93°$, $[\alpha] = -61{\cdot}9°$, $[M] = -413°$. These were united and converted into the hydrochloride as before by the action of calcium chloride solution. A crop of the anhydrous and optically pure *l*-hydrochloride was thus obtained (Found: Pt, 42·2%). A 1·328% aqueous solution had $\alpha = -5{\cdot}72°$, $[\alpha] = -108°$, and $[M] = -498°$.

d-*Tetrachloro*(*triaminopropane-mono*-l-*camphor*-β-*sulphonate*)*platinum Semihydrate*.—This was prepared in precisely the same way as the *l*-base *d*-sulphonate, the racemic hydrochloride being treated in solution with silver *l*-camphor-β-sulphonate. The product was recrystallised as before six times from water, and the final crop had in 1·366% aqueous solution, $\alpha = +3{\cdot}47°$, whence $[\alpha] = +63{\cdot}5°$ and $[M] = +424°$ (Found: Pt, 29·15%).

Once again an optically impure crop of the opposite enantiomorph could be obtained by precipitation with alcohol. The filtrate from the second fraction of the *l*-sulphonate, when diluted considerably with alcohol, deposited a crop of the sulphonate which, when separated and dried, had, in 1·218% aqueous solution, $\alpha = -2{\cdot}59°$, whence $[\alpha] = -53{\cdot}1°$ and $[M] = -355°$. No further attempts to complete the resolution of this crop by solution in water and reprecipitation with alcohol were made.

d-*Tetrachloro*(*triaminopropane-monohydrochloride*)*platinum*.—The optically pure, sixth fraction of the *d*-base *l*-sulphonate, having $[M] = +424°$, was treated as before in cold aqueous solution with calcium chloride, and the *d*-tetrachloro(triaminopropane-monohydrochloride)platinum separated in fine crystals, which were filtered off, washed with alcohol and ether, and dried. These crystals, like the *l*-hydrochloride, were anhydrous (Found: Pt, 42·1%), and darkened at 260—265° and melted at 277—278° (decomp.). A 1·555% aqueous solution had $\alpha^{15°}_{5780} = +5{\cdot}80°$, whence $[\alpha]^{15°}_{5780} = +93{\cdot}2°$, $[M]^{15°}_{5780} = +431°$, and $\alpha^{15°}_{5461} = +6{\cdot}73°$, whence $[\alpha]^{15°}_{5461} = +108°$, $[M]^{15°}_{5461} = +501°$.

As before, the initial filtrate from the first crude crop of the *l*-camphorsulphonate slowly deposited a small quantity of the almost optically pure *d*-base *l*-sulphonate in long, pale lemon-yellow

needles. These, after being washed and dried, had in 1·232% aqueous solution $\alpha = +3{\cdot}11°$, whence $[\alpha] = +63{\cdot}1°$ and $[M] = +421°$. There was not sufficient of this material, however, for conversion into the *d*-hydrochloride.

*Tetrachloro(triaminopropane-mono-*d*-α-bromocamphor-π-sulphonate)platinum*, $[Cl_4PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2,C_{10}H_{14}OBr{\cdot}SO_3H]$. —The bromocamphorsulphonate was obtained by mixing hot aqueous solutions of the monohydrochloride (10 g.) and of silver *d*-bromocamphorsulphonate (6·8 g.). The mixed solution, when boiled, filtered, concentrated, and chilled, gave the bromocamphorsulphonate in fine, canary-yellow crystals. These, after being once recrystallised from water and dried, melted at 271—273° (decomp.) (Found: C, 21·0; H, 3·6; Pt, 26·6. $C_{13}H_{26}O_4N_3Cl_4BrSPt$ requires C, 21·15; H, 3·55; Pt, 26·5%). The sulphonate in 1·916% aqueous solution had $\alpha = +3{\cdot}52°$, $[\alpha] = +45{\cdot}9°$, and $[M] = +339°$. This material was now recrystallised three more times from water and, in 1·320% solution, then had $\alpha = +2{\cdot}48°$, $[\alpha] = +47{\cdot}0°$, $[M] = +346°$. Since ammonium *d*-bromocamphor-π-sulphonate has $[M]^{22°}_{5461} = +347°$ (Pope and Read, J., 1910, **97**, 2201), it was obvious that the activity of the platinum compound was due to the bromocamphorsulphonate ion alone, and that no apparent resolution was being effected.

Trichlorotriaminopropaneplatinic Chloride,

$$[Cl_3PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2]Cl.$$

—A cold aqueous solution of tetrachloro(triaminopropane-monohydrochloride)platinum was treated with an excess of ammonia solution (*d* 0·966). The fine, yellow, crystalline precipitate which soon appeared was very sparingly soluble in cold water; when boiled with hot water, it slowly dissolved, but the production of a red colour showed considerable reduction to a platinous salt. This ready reduction of co-ordinated platinic to platinous compounds has already been noted by Werner (*Vierteljahrs. Naturfors. Ges. Zurich*, 1917, **62**, 553). The compound was therefore filtered off, and thoroughly washed with cold water, alcohol, and ether, and *trichlorotriaminopropaneplatinic chloride* was thus obtained in fine, yellow crystals which began to darken at about 210° and melted at 242—243° (decomp.) (Found: C, 8·4; H, 2·8; N, 10·1; Pt, 45·9. $C_3H_{11}N_3Cl_4Pt$ requires C, 8·45; H, 2·6; N, 9·9; Pt, 45·8%). The same compound was also obtained when the original monohydrochloride was treated in solution with either one or two molecules of ethylenediamine hydrate.

Tetrachloro(triaminopropane-hydrogen-oxalate)platinum,

$$[Cl_4PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2,(CO_2H)_2].$$

—This compound rapidly separated when an aqueous solution of the

monohydrochloride was treated with a solution of oxalic acid: it is only slightly soluble in cold water, and when filtered off, washed with water, alcohol, and ether, was obtained as a fine, pale yellow powder, m. p. 248—251° (decomp.) (Found: N, 8·4; Cl, 27·7; Pt, 37·6. $C_5H_{13}O_4N_3Cl_4Pt$ requires N, 8·1; Cl, 27·5; Pt, 37·8%).

Monochloromono-oxalatotriaminopropaneplatinic Chloride, $[Cl(CO{\cdot}O)_2PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2]Cl$. —Solutions of tetrachloro(triaminopropane-monohydrochloride)-platinum (9·9 g.) and hydrated oxalic acid (5·2 g.; 2 mols.), each in 125 c.c. of water, were mixed, and the solution was heated to dissolve the precipitated hydrogen oxalate salt. The clear solution was boiled under reflux for 10 hours, and on filtering and cooling deposited fine, yellow crystals. These were twice recrystallised from hot water, in which they were freely soluble, and the *monochloromono-oxalatotriaminopropaneplatinic chloride* was thus obtained as a pale brownish-yellow, microcrystalline powder, which decomposed with foaming between 200° and 210° and was then slowly transformed to a dry, black mass (Found: N, 9·6; Cl, 16·2; Pt, 43·85. $C_5H_{11}O_4N_3Cl_2Pt$ requires N, 9·5; Cl, 16·0; Pt, 44·0%).

Many attempts were made to reduce the monohydrochloride to a compound of bivalent platinum of the type of dichloro(triaminopropane-monohydrochloride)platinum, $[Cl_2PtNH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}NH_2,HCl]$, a compound which should also have been susceptible to resolution into optically active forms. The yellow monohydrochloride, when treated in hot aqueous solution with sulphur dioxide, slowly underwent reduction with the production of a colourless solution. From this solution various products were obtained, but all on attempted recrystallisation from water underwent decomposition with the evolution of sulphur dioxide, and no well-defined, stable compound could be isolated.

The author is greatly indebted to Professor Sir William Pope, F.R.S., for supplies of platinum and of *l*-camphor, without which this investigation could not have been carried out.

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CLXIX.—*Sugar Carbonates. Part III. Derivatives of γ-Methylfructoside, γ-Ethylfructoside, and Normal Methylfructoside.*

By Charles Frederick Allpress, Walter Norman Haworth, and John James Inkster.

Since the fructose residue in sucrose is not the normal, but the γ- or labile form, it seems to be a necessary preliminary to the synthesis of sucrose that derivatives of γ-methylfructoside should be made available. The fructoside is readily prepared from ordinary fructose by standard methods, and is characterised by the ease with which its methyl residue can be eliminated. This property induced us to attempt to substitute carbalkyloxy-groups for the hydrogen atoms of the remaining hydroxyls in γ-methylfructoside, and in this we have succeeded. The methods employed are described below, but we have not yet been successful in exposing the reducing hydroxyl group of the substituted ketose. Similar experiments have also been undertaken with *γ-ethylfructoside*.

Condensation of γ-methylfructoside with methyl chloroformate in presence of pyridine gave rise to *tetracarbomethoxy γ-methylfructoside*. A series of experiments on the graded hydrolysis of this compound with aqueous-alcoholic solutions containing 0·5% up to 2·5% of hydrogen chloride gave distinct evidence of hydrolysis as indicated by the Fehling's test, and although the methoxyl content of the product (28% OMe) approximated to that (30·1% OMe) required for tetracarbomethoxy γ-fructose, yet the other analytical data showed that the product was not homogeneous. The corresponding *tetracarbethoxy γ-methylfructoside* was also prepared.

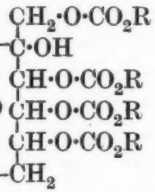
Condensation of γ-ethylfructoside with ethyl chloroformate gave *tetracarbethoxy γ-ethylfructoside*, which distilled without difficulty and showed $[\alpha]_D + 27{\cdot}5°$ in ethyl alcohol. The dextrorotatory character of the product would appear to indicate that the γ-ethylfructoside residue has been retained, and indeed the compound gave the usual test with neutral permanganate, which was decolorised instantly. Hydrolysis of the glucosidic ethoxyl residue was not effected completely by heating with 1·25% aqueous hydrogen chloride for 3 hours at 80°, but seemed to proceed with greater ease at 90°, and the product reduced Fehling's solution normally; we have, however, not yet isolated pure tetracarbethoxy γ-fructose. The results of our experiments indicate that the introduction of carbonic ester residues into the γ-fructosides tends considerably to increase the stability of the alkylfructoside residue.

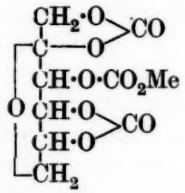
Compounds of the desired type but related to normal fructose

have already been described (Allpress and Haworth, J., 1924, **125**, 1228). These are tetracarbomethoxy fructose and tetracarbethoxy fructose, and both these compounds are represented on the basis of the revised structural formula for normal fructose (I). It was previously stated that, although these two crystalline products displayed little, if any, mutarotation in chloroform or acetone, they were probably to be formulated as containing a free reducing group. This conclusion has now been confirmed by the preparation of the corresponding methylfructosides by methylation. These are devoid of action on Fehling's solution, and are recognised as *tetracarbomethoxy methylfructoside* and *tetracarbethoxy methylfructoside*. The carboxylated methylfructosides of the two structural types, the stable and the unstable form, are therefore made available.

In the γ- or unstable series we have not encountered an example of the formation of a true carbonate of the type represented by (II) derived from the normal fructose. The formulation of this crystalline substance, monocarbomethoxy fructose dicarbonate, is, however, now revised on the basis of the new fructose formula (compare Allpress and Haworth, *loc. cit.*).

(I.)





(II.)

Experimental.

Tetracarbomethoxy γ-Methylfructoside.—To a well-cooled mixture of γ-methylfructoside (13 g.; prepared by Menzies' method, J., 1922, **121**, 2238) and dry chloroform containing pyridine (6 mols.), methyl chloroformate was gradually added. The γ-methylfructoside dissolved after agitation for several hours and the reaction was then at an end. Chloroform was removed under diminished pressure, pyridine hydrochloride extracted with water, and the remaining syrup was dissolved in acetone, dried, and distilled after removal of the solvent (b. p. 226—227°/0·1 mm.). Yield, 10—14 g. *Tetracarbomethoxy γ-methylfructoside* was thus obtained as a pale yellow, viscid syrup which showed no tendency to crystallise and did not reduce Fehling's solution. It had $[\alpha]_D$ + 19·8° in acetone (c = 1·5) (Found : C, 42·2; H, 5·1; OMe, 33·5; *M*, ebullioscopic in acetone, 415. $C_{15}H_{22}O_{14}$ requires C, 42·3; H, 5·2; OMe, 36·4%; *M*, 426). The compound displayed unexpected stability towards boiling 0·5% aqueous-alcoholic hydrogen chloride; although the product reduced Fehling's solution, it consisted largely of the unaltered fructoside.

Tetracarbethoxy γ-Methylfructoside.—The above procedure being imitated throughout, γ-methylfructoside (3·6 g.) was condensed with ethyl chloroformate, and the product (5·2 g.), consisting of a pale yellow syrup, was twice distilled (yield, 3·8 g.); b. p. 235—238°/0·07 mm., $[\alpha]_D$ + 22·5° in ethyl alcohol. It was devoid of action towards Fehling's solution, but readily reduced cold neutral permanganate (Found: C, 46·8; H, 6·2; OR, 41·9.* $C_{19}H_{30}O_{14}$ requires C, 47·3; H, 6·2; OR,* 43·8%).

This product was submitted to hydrolysis with aqueous-alcoholic hydrogen chloride, and it appeared that with concentrations of acid below 1% no significant change occurred on heating at 80° for 3 hours. Concentrations of acid varying from 1·75% to 2% gave rise to a product which reduced Fehling's solution actively and showed a diminution of rotation to a value which remained constant during several hours.

γ-Ethylfructoside.—Dried ethyl alcohol containing 0·5% of hydrogen chloride was mixed with dried and sieved fructose (1·25 g. for each 100 c.c. of solution), and the solution was observed polarimetrically:

Time (mins.)	0	3	5	7	10	13	18
$[\alpha]_D^{17°}$	−55°	−9·5°	+3°	+10·5°	15·5°	16·5°	17·5°
Time (mins.)	24	27	30	36	47	65	
$[\alpha]_D^{17°}$	17·5°	17·5°	16·5°	16·5°	15·5°	14·5°	

The rotation thus became positive after about 4 minutes, and attained a maximum rotation in 18 to 27 minutes from the time of adding the acid. After this the value slowly decreased, and became negative after several hours.

The following procedure was adopted for the preparation of larger quantities. Fructose (7·5 g.) was shaken with pure ethyl alcohol (500 c.c.) for an hour. Thereafter, alcohol containing hydrogen chloride was added in such quantity as to give a concentration of 0·5% of hydrogen chloride, and this mixture was shaken for 25 minutes, a clear solution being obtained. At this stage the condensation was arrested by neutralising the acid with sodium ethoxide dissolved in dry alcohol. Silver carbonate was then added, which removed the last traces of hydrogen chloride. Filtration and evaporation under diminished pressure yielded a syrup, from which the last traces of alcohol were removed by heating at 80° in a high vacuum. The product, which contained a small quantity of sodium chloride, was extracted four times with boiling ethyl acetate, and the extract yielded on evaporation of the solvent a clear syrup which hardened on cooling. The last traces of solvent were removed by heating for an hour at 100° under 0·05 mm. pressure.

* OR calculated as 4OEt + 1OMe.

The *γ-ethylfructoside* was readily soluble in water, alcohol, acetone, or pyridine, and showed in alcohol $[\alpha]_D + 28°$. It was devoid of any action towards Fehling's solution except after prolonged boiling, but decolorised neutral permanganate readily (Found: C, 45·7; H, 7·8. $C_8H_{16}O_6$ requires C, 46·2; H, 7·7%).

Tetracarbethoxy γ-Ethylfructoside.—A solution of γ-ethylfructoside (1 mol.) in dry pyridine (7 mols.) was diluted with four times its volume of dry chloroform and cooled to 0°. A chloroform solution of ethyl chloroformate was then added gradually with stirring. After being kept at room temperature for an hour, the solvent was removed under diminished pressure, and the pyridine hydrochloride, which crystallised, was extracted with water. The viscid, yellow residue was dissolved in acetone, reprecipitated by water, and again dissolved in acetone; this solution was dried over magnesium sulphate, and the solvent distilled; the residue, in the absence of traces of pyridine hydrochloride, distilled without difficulty; b. p. 228°/0·05 mm.

The *tetracarbethoxy γ-ethylfructoside* showed in ethyl alcohol, $[\alpha]_D + 27·5°$. It was also soluble in acetone and chloroform. It was not affected by Fehling's solution, but decolorised neutral permanganate (Found: C, 48·3; H, 6·45; OEt, 43·2. $C_{20}H_{32}O_{14}$ requires C, 48·4; H, 6·45; OEt, 45·3%). Towards aqueous-alcoholic hydrogen chloride, this completely substituted derivative of γ-ethylfructoside behaved like the corresponding derivative of γ-methylfructoside, and showed considerable stability even at 100°. Hydrolysis of the glucosidic ethyl group was therefore considerably retarded by the introduction of the carbethoxy-groups.

The Normal Forms of Tetracarbomethoxy Methylfructoside and Tetracarbethoxy Methylfructoside.—*Tetracarbomethoxy methylfructoside* was prepared by subjecting tetracarbomethoxy fructose (m. p. 126°) to two methylations by Purdie's reagents. The isolated product was crystallised from ethyl acetate; it melted at 107° and showed $[\alpha]_D$ −126·1° in chloroform ($c = 0·6$) (Found: C, 42·3; H, 4·9; OMe, 34·2. $C_{15}H_{22}O_{14}$ requires C, 42·3; H, 5·2; OMe, 36·4%). *Tetracarbethoxy methylfructoside*, prepared by methylating tetracarbethoxy fructose (m. p. 118°) with Purdie's reagents, did not crystallise and showed $[\alpha]_D$ −90·9° in acetone ($c = 1·2$) (Found: C, 47·1; H, 6·1. $C_{19}H_{30}O_{14}$ requires C, 47·3; H, 6·2%).

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CLXX.—*The Study of Lactones Derived from Simple Sugars.*

By HARRY DUGALD KEITH DREW, EDWARD HAGUE GOODYEAR, and WALTER NORMAN HAWORTH.

THE investigations of one of us and his collaborators have furnished evidence that the aldoses and ketoses tend to exist normally as amylene oxides, whilst the less stable or γ-forms of sugars appear to be butylene oxides (compare J., 1926, 89, 1858, 2303).

One of the conclusions leading to this fundamental generalisation may be expressed by the statement that the lactones derived from the fully methylated normal sugars are the δ-lactones, whilst the lactones from the γ-forms of these sugars are the more stable γ-lactones; and it has already been shown (*loc. cit.*, p. 89) that a comparison of the relative degrees of stability of the two lactones derived from a given sugar enables each of them to be classified as a γ- or a δ-lactone, and thence reveals the ring structure of each parent sugar form.

The method adopted for comparing the lactones was that of observing the mutarotation–time curves for aqueous solutions, the relative slopes of the curves derived from a pair of lactones enabling each member of the pair to be classified as a γ- or a δ-lactone. When, however, the specific rotations of the free acids in the same solvent are known, a direct comparison of the rate of change of each lactone into the corresponding acid can be made by means of a simple calculation, and the result exhibited in the form of a curve.

This method has the advantage of eliminating the unequal effects due to the rotations of the two methylated acids derived from a pair of lactones; and for this reason we have now determined the specific rotations of a number of acids derived from the γ- and δ-forms of trimethylated pentoses and tetramethylated hexoses, and have plotted the hydration curves of the respective lactones.

In the determination of specific rotation of the acids, a lactone was dissolved in the equivalent of $N/10$-sodium carbonate, and the solution was heated until transformation to the sodium salt was complete. After being cooled, the solution was rapidly neutralised with $N/10$-sulphuric acid and its rotation was then observed at intervals. Extrapolation, where necessary, gave a value for the specific rotation of the pure acid.

The values so obtained are probably not strictly accurate, on account of the presence in the solution of a half-molecular proportion of sodium sulphate, which may modify the rotatory power

(compare Clough, J., 1914, **105**, 49; 1915, **107**, 96, 1509). They are considered sufficiently exact, however, to be applicable to the present purpose.

Other effects which cannot easily be allowed for in the observation of mutarotation values of the lactones are the effect of variation of concentration and that of variation in specific rotation of the lactone due to the presence of an increasing proportion of acid. These effects are probably only of a secondary order of magnitude.

With this reservation, then, the percentage of acid present at a given time during the hydration of a lactone is calculable from the expression $100(R - R_l)/(R_a - R_l)$, where R is the specific rotation of the solution at the given time and R_a and R_l are the specific rotations of the lactone in the form of acid and the lactone, respectively. (If r_a represents the true specific rotation of the acid, then $R_a = r_a M_a/M_l$, where M_a and M_l are respectively the molecular weights of acid and lactone.) This expression has also been employed by Levene and Simms (*J. Biol. Chem.*, 1925, **65**, 46).

Table I shows the values of the specific rotations of those lactones which have been studied and of their acids; and the accompanying diagram exhibits in each case the rate of change of lactone to acid in aqueous solution at the ordinary temperature.

TABLE I.

Parent sugar.	Specific rotation of lactone (R_l). $[\alpha]_{5461}$.	$[\alpha]_D$.	Conc.	Specific rotation of acid (r_a). $[\alpha]_{5461}$.	$[\alpha]_D$.	Conc.
d-2 : 3 : 5 : 6-Tetramethyl glucose	+ 72°	+ 63°	1·42	+31·8°	+27·7°	1·08
d-2 : 3 : 4 : 6- „ „	+113	+ 98	1·56	+25·5	+22	1·09
d-2 : 3 : 5 : 6-Tetramethyl galactose ...	− 31	− 27	1·47	− 8·3	− 8·0	0·90
d-2 : 3 : 4 : 6- „ „ ...	+191	+166·5	1·89	+25·5	+22	1·23
d-2 : 3 : 5 : 6-Tetramethyl mannose ...	+ 73	+ 63	2·51	−27	−23	0·92
d-2 : 3 : 4 : 6- „ „ ...	+172	+150	1·88	+15·8	+13·7	1·12
l-2 : 3 : 5-Trimethyl xylose	+ 85	+ 74	1·11	+34·4	+29	1·11
l-2 : 3 : 4- „ „	± 0	± 0	1·87	+29·9	+26	0·98
l-2 : 3 : 5-Trimethyl arabinose	− 51	− 44	1·06	− 3·4	− 2·9	0·82
l-2 : 3 : 4- „ „	+206	+180	1·41	+14·6	+13·8	0·72

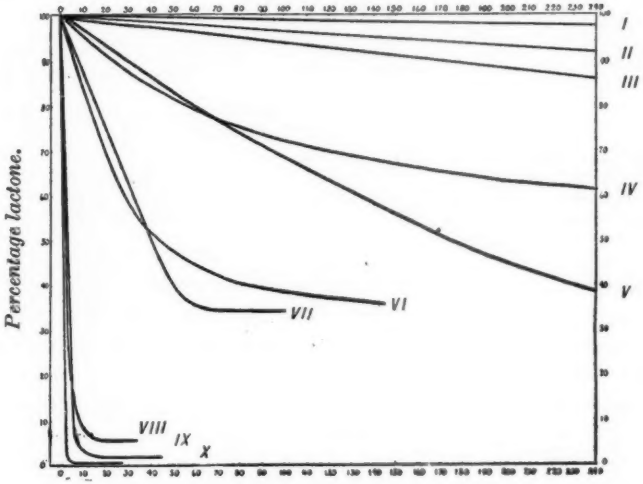
It will be observed that, in the case of each separate pair of lactones derived from a normal and a γ-form of the same sugar, the curve representing the rate of formation of γ-hydroxy-acid from γ-lactone is sharply distinguished from that representing the rate of formation of the δ-hydroxy-acid from δ-lactone, the latter being much the steeper. These results amply confirm the conclusions arrived at in the former paper (Charlton, Haworth, and Peat, J., 1926, 89). Further, the whole of the curves being taken into consideration, each of the δ-lactone curves is steeper than any γ-lactone curve—a striking fact when the differences in configuration throughout the series are considered.

Between the two extreme types of curve, *viz.*, the very steep

δ-lactone curves and the very flat γ-lactone curves, are found two less steep δ-lactone curves (trimethyl δ-xylono- and tetramethyl δ-mannono-lactones) and two less flat γ-lactone curves (trimethyl γ-arabono- and trimethyl γ-glucono-lactones). These modifications in the form of the hydration curves are obviously connected with the configurations of the lactones. Further physico-chemical methods are being brought to bear upon the interpretation of this phenomenon.

FIG. 1.

Comparative rates of hydrolysis of the lactones.



Time in hours.

I *Tetramethyl γ-mannonolactone.* II *Tetramethyl γ-galactonolactone.*
III *Trimethyl γ-xylonolactone.* IV *Trimethyl γ-arabonolactone.*
V *Tetramethyl γ-gluconolactone.* VI *Tetramethyl δ-mannonolactone.*
VII *Trimethyl δ-xylonolactone.* VIII *Tetramethyl δ-gluconolactone.*
IX *Tetramethyl δ-galactonolactone.* X *Trimethyl δ-arabonolactone.*

Since the equilibrium values of all the lactones cannot be observed with much accuracy owing to the extreme length of time required in some instances, it is interesting to compare the times in which a quarter (say) of the lactone is changed to acid in the various cases. These are shown in Table II.

TABLE II.

	γ-Lactones. 25% Acid developed in (hrs.).	δ-Lactones. 25% Acid developed in (hrs.).
Tetramethyl glucono-	75	<1
Tetramethyl galactono-	600	1
Tetramethyl mannono-	(this stage is not reached)	17
Trimethyl xylono-	430	22
Trimethyl arabono-	60	<1

The results do not support the generalisation arrived at by Levene and Simms (*loc. cit.*), that the rates of lactone formation among normal hexose acids are practically identical. The speeds of the lactone ⟶ acid and acid ⟶ lactone reactions are considerably affected by the configuration of the sugar.

Table III shows the approximate proportions of acid and lactone at equilibrium, where these have been measured or calculated from the curves. The ratios of these values give the relative speed constants for the acid ⟶ lactone change.

TABLE III.

	γ-Lactones. Acid : lactone at equil.			δ-Lactones. Acid : lactone at equil.		
			Attained in (hrs.).			Attained in (hrs.).
Tetramethyl glucono-	87	13	520	95	5	5
Tetramethyl galactono- ...	—	—	—	98·5	1·5	18
Tetramethyl mannono- ...	11	89	>900	64	36	140
Trimethyl xylono-	31	69	>500	65	35	70
Trimethyl arabono-	45	55	>500	99·5	0·5	4

In many cases (see experimental section), we have re-determined the mutarotation curves of the lactones, using material which is seen, in some instances, to be substantially purer than that hitherto obtained. Thus, three lactones (trimethyl δ-arabono-, tetramethyl δ-mannono-, and tetramethyl γ-glucono-), which were previously known only as syrups, have been obtained in the crystalline condition. In all, six of the ten lactones examined are crystalline. In two of these cases, the specific rotation shows marked enhancement of the former values.

The initial material in the preparation of tetramethyl δ-mannonolactone was pure α-methylmannoside, which was methylated to tetramethyl α-methylmannoside, obtained in a pure crystalline condition. Hydrolysis yielded 2 : 3 : 4 : 6-*tetramethyl mannose*, having $[\alpha]_D^{18°}$ +26° in methyl alcohol (c = 5·15), rising at equilibrium to +31°. Irvine and Moodie's product (J., 1905, **87**, 1462) had $[\alpha]_D^{20°}$ +14·6° in methyl alcohol (c = 5), rising to +17·2° at equilibrium.

Oxidation of tetramethyl mannose gave the crude syrupy lactone, which, after transformation to the *phenylhydrazide*, followed by crystallisation and recovery, gave 2 : 3 : 4 : 6-*tetramethyl mannonolactone* in colourless, prismatic needles (m. p. 23—25°), having $[\alpha]_D^{18°}$ +150° in water (c = 1·88); and $[\alpha]_D^{20°}$ +130·5°, falling to $[\alpha]_D^{20°}$ +34° in 14 days, in 60% methyl alcohol (c = 1·489). Irvine and Miss B. M. Paterson (J., 1914, **105**, 915) describe a liquid product having $[\alpha]_D^{20°}$ +78·8°, falling to +38·5° in 10 days, in 60%

methyl alcohol ($c = 1{\cdot}384$), as the above lactone, but quote an inconclusive analytical result for carbon and do not record a value for methoxyl. Their product was obviously impure. The same remark can be applied to the syrup obtained by Levene and Meyer (*J. Biol. Chem.*, 1924, **60**, 167), which had $[\alpha]_D$ +105° in water ($c = 2{\cdot}85$) and gave poor analytical values.

We have repeated the preparation of the 2 : 3 : 5 : 6-tetramethyl mannonolactone described by Levene and Simms (*loc. cit.*), who record an inconclusive analysis; and have found that another product accompanies the lactone under the experimental conditions employed by these authors. The homogeneity of this lactone is therefore under suspicion, and test experiments are in progress to decide the point. In the meantime, the figures recorded in this paper should be regarded as provisional in the case of this lactone and also of the trimethyl γ-xylonolactone. It seems doubtful whether a pure specimen of a completely methylated lactone is readily obtainable by direct methylation of the lactone of a hexonic or pentonic acid. Pure specimens we have handled have been prepared by oxidation of a methylated sugar.

In the case of arabinose, the observations were conducted on the crystalline 2 : 3 : 4-trimethyl δ-arabonolactone (m. p. 45°) isolated as described by Drew and Haworth (this vol., p. 778).

2 : 3 : 5 : 6-Tetramethyl γ-gluconolactone was similarly obtained as a crystalline solid (m. p. 26—27°), having $[\alpha]_D^{21°}$ +62·5° in water ($c = 1{\cdot}415$), a value which substantially agrees with that recorded by Charlton, Haworth, and Peat (*loc. cit.*), *viz.*, $[\alpha]_D$ +61·5°.

In a further paper (*J. Biol. Chem.*, 1926, **68**, 737), Levene and Simms record for tetramethyl δ-gluconolactone a specific rotation of $[\alpha]_D^{22°}$ +108° in water, and for the corresponding equilibrium solution a specific rotation of $[\alpha]_D^{22°}$ +46°; whereas Charlton, Haworth, and Peat (*loc. cit.*) record values of $[\alpha]_D$ +101° and $[\alpha]_D$ +25·6°, respectively. We have now examined two separately prepared specimens of this lactone, and have obtained specific rotations of $[\alpha]_D^{19°}$ +98° for the lactone in water and $[\alpha]_D^{19°}$ +28° for the equilibrium solution. The specific rotation of the acid in water was observed to be $[\alpha]_D^{19°}$ +22° ($c = 1{\cdot}09$) and $[\alpha]_D^{20°}$ +28° ($c = 0{\cdot}9$) for the two samples, as against Levene and Simms's value of $[\alpha]_D$ +40·5°. It is therefore considered that the figure obtained by Levene and Simms is of doubtful accuracy.

Experimental.

Tetramethyl γ-Gluconolactone.—Tetramethyl γ-glucose, oxidised at 75° by means of bromine, gave the *lactone* as an oil ($n_D^{14°}$ 1·4501)

which solidified in colourless needles, m. p. 26—27° (Found : C, 51·0; H, 7·6. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%).

In water ($c = 1·415$), the following rotations were observed :

Time (hrs.).	$[\alpha]^{20°}_{5461}$.	% Lactone present.	Time (hrs.).	$[\alpha]^{20°}_{5461}$.	% Lactone present.
0	+72°	100	240	+48·8°	38·7
73·7	62·3	76	360	42·4	21·8
121·2	58·3	63·7	408	40·7	17·4
144	55·9	57·4	501	38·8	12·4
192	51·6	46			(constant)

For the lactone : $[\alpha]^{21°}_{5461}$ +72°, $[\alpha]^{21°}_{5780}$ +65°, $[\alpha]^{21°}_{D}$ +62·5°. For the acid (calculated as lactone) : $[\alpha]^{20°}_{5461}$ +34°, $[\alpha]^{20°}_{D}$ +30° (in water, $c = 1·08$), rising after 4 days to $[\alpha]^{19°}_{5461}$ +41°.

Tetramethyl δ-Gluconolactone.—In water ($c = 1·564$), the lactone gave the rotations :

Time (hrs.).	$[\alpha]^{19°}_{5461}$.	% Lactone present.	Time (hrs.).	$[\alpha]^{19°}_{5461}$.	% Lactone present.
0	+112·5°	100	0·58	+95°	79·4
0·12	109	95·9	0·68	91·5	75·3
0·25	105	91·2	1·33	73	53·6
0·33	101·5	86·5	1·82	59	37·1
0·45	100	85·3	16·75	32	5·4
					(constant)

For the acid (calculated as lactone) : $[\alpha]^{19°}_{5461}$ +27·4° in water ($c = 1·095$), rising after 6 days to $[\alpha]^{19°}_{5461}$ +33·8°.

Tetramethyl γ-Galactonolactone.—For this lactone, Haworth, Ruell, and Westgarth (*loc. cit.*) give $[\alpha]_D$ −27° for the initial value in water ($c = 1·47$), changing after 12 days to $[\alpha]_D$ −25°. Thus, 89·7% of lactone is still present after 12 days, the acid (calculated as lactone) having $[\alpha]^{16°}_{D}$ −8·6° in water ($c = 0·896$). It seems improbable, therefore, that equilibrium had been attained in the period indicated. Further experiments in this connexion are in progress.

Tetramethyl δ-Galactonolactone.—The following values were observed for the lactone in water ($c = 1·891$) :

Time (hrs.).	$[\alpha]^{21°}_{D}$.	% Lactone present.	Time (hrs.).	$[\alpha]^{21°}_{D}$.	% Lactone present.
0	+166·5°	100	3·0	+69·5°	32·0
1·5	114·5	63·5	4·25	47·8	16·8
2·5	84·7	42·7	21·0	26·2	1·7
					(constant)

For the acid (calculated as lactone) : $[\alpha]^{21°}_{D}$ +24° in water ($c = 1·228$), rising after 48 hours to $[\alpha]^{21°}_{D}$ +26·3° (compare Haworth, Ruell, and Westgarth, J., 1924, **125**, 2473; Pryde, Hirst, and Humphreys, J., 1925, **127**, 355.

Tetramethyl γ-Mannonolactone.—A sample of the lactone (m. p.

106—107°), prepared by Levene and Simms's process (*loc. cit.*), gave an initial rotation of $[\alpha]_D^{19°}$ +63° in water ($c = 2{\cdot}51$), falling during 9 days to $[\alpha]_D^{20°}$ +61°. Catalysis with hydrochloric acid gave an equilibrium rotation of $[\alpha]_D^{20°}$ +53°. For the acid, in water ($c = 0{\cdot}923$): $[\alpha]_D^{21°}$ −23°, becoming $[\alpha]_D^{21°}$ −17° after 5 days. It is clear, therefore, that the mutarotation of the lactone is extremely slow. Further work is in progress to test the purity of the lactone and to determine the equilibrium composition of the aqueous solution.

2 : 3 : 4 : 6-*Tetramethyl* δ-*Mannonolactone.*—Pure α-methylmannoside was methylated by means of sodium hydroxide and methyl sulphate, and then by means of silver oxide and methyl iodide. The product (b. p. 105°/0·03 mm.; $n_D^{16°}$ 1·4494) solidified in crystals of tetramethyl α-methylmannoside, m. p. 38—40°. The mannoside was hydrolysed by 5% hydrochloric acid to 2 : 3 : 4 : 6-*tetramethyl mannose*, obtained as a colourless syrup (b. p. 114·5°/0·035 mm.; $n_D^{19°}$ 1·4597). The overall yield of pure product was 50% (Found: OMe, 50·5. $C_{10}H_{20}O_6$ requires OMe, 52·5%). The sugar had $[\alpha]_D^{18°}$ +26° in methyl alcohol ($c = 5{\cdot}15$), rising to +31° at equilibrium.

The tetramethyl mannose, on oxidation at 45° with bromine, yielded the crude lactone as a colourless syrup (b. p. 117°/0·04 mm.; $n_D^{17°}$ 1·4643; $[\alpha]_{5461}^{19°}$ +156° in water). Since the analytical figures (C, 50·7; H, 7·8; OMe, 48·8, 49·3%) indicated the presence of appreciable impurity, the whole was converted into the *phenylhydrazide*, white, nacreous flakes from benzene; m. p. 184—185° (Found: C, 56·0; H, 7·6; N, 8·4; OMe, 35·0. $C_{16}H_{26}O_6N_2$ requires C, 56·1; H, 7·6; N, 8·2; OMe, 36·3%). The recrystallised phenylhydrazide was hydrolysed by means of 1% hydrochloric acid, and the *lactone* recovered as a syrup (b. p. 104°/0·02 mm.; $n_D^{16°}$ 1·4650), which solidified in colourless, prismatic needles, m. p. 23—25° after being drained on porous tile in a vacuum (Found: C, 51·2; H, 7·8; OMe, 50·5. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7; OMe, 53·0%).

In water ($c = 1{\cdot}88$) the following rotations were observed:

Time (hrs.).	$[\alpha]_{5461}^{19°}$.	% Lactone present.	Time (hrs.).	$[\alpha]_{5461}^{19°}$.	% Lactone present.
0	+172°	100	34·3	+102°	54·8
0·3	171	99·4	57·1	88	45·8
5·8	157·5	90·6	71·1	82·5	42·3
9·3	148	84·5	146·3	73·4	36·0 (constant)

For the lactone: $[\alpha]_{5461}^{18°}$ +172·3°, $[\alpha]_{5780}^{18°}$ +153°, $[\alpha]_D^{18°}$ +150°. For the acid (calculated as lactone): $[\alpha]_{5461}^{14°}$ +17°, $[\alpha]_D^{14°}$ +14·8 in water ($c = 1{\cdot}12$), rising after 88 hours to $[\alpha]_{5461}^{18°}$ +60·7°.

Trimethyl γ-Xylonolactone.—The records of Haworth and Westgarth (J., 1926, 886) give the following mutarotation figures for the lactone in water ($c = 1{\cdot}106$) : *

Time (hrs.)	0	64	168	504
$[\alpha]_D$	+74°	+71·8°	+69·6°	+61·4°
% Lactone present	100	94·6	89·4	70·0

For the acid (calculated as lactone), we observed $[\alpha]_D^{16°}$ +31·7° in water ($c = 0{\cdot}944$), rising after 17 hours to $[\alpha]_D^{16°}$ +33·5° (equilibrium not attained).

Trimethyl δ-Xylonolactone.—Pure trimethyl methylxyloside (m. p. 46—48°) was hydrolysed by means of 3% hydrobromic acid, and the resulting sugar oxidised at 75° with bromine. The lactone (b. p. 101°/0·04 mm.) at once solidified. It crystallised from petroleum in long, colourless needles, m. p. 56° [Found : C, 50·75; H, 7·2; OMe, 48·9; *M*, ebullioscopic in benzene, 200 ($c = 0{\cdot}93$). $C_8H_{14}O_5$ requires C, 50·5; H, 7·4; OMe, 48·9%; *M*, 190] (compare Haworth and Westgarth, *loc. cit.*). In water ($c = 1{\cdot}871$) the lactone gave :

Time (hrs.).	$[\alpha]_{5461}^{20°}$.	% Lactone present.	Time (hrs.).	$[\alpha]_{5461}^{20°}$.	% Lactone present.
0	± 0°	100	32·75	+13·3°	59·1
6·75	+ 2·4	92·7	46·75	17·4	46·8
22·25	8·8	73·1	70·75	21·4	34·6 (constant)

For the acid (calculated as lactone) : $[\alpha]_{5461}^{16°}$ +32·7° in water ($c = 0{\cdot}977$), falling after 8 hours to $[\alpha]_{5461}^{15°}$ +21·5°.

2 : 3 : 5-*Trimethyl γ-Arabonolactone.*—The following values are taken from the record of Haworth and Nicholson (J., 1926, 1902).

Time (hrs.).	$[\alpha]_D$.	% Lactone present.	Time (hrs.).	$[\alpha]_D$.	% Lactone present.
0	−44·4°	100	168	−30·0°	65·0
2	43·8	98·5	288	27·0	57·8
24	40·0	89·3	480	25·2	53·4
120	32·1	70·1			

For the acid (calculated as lactone), we observed $[\alpha]_D^{16°}$ −3°, rising after 40 hours to $[\alpha]_D^{15°}$ −15° (equilibrium not attained).

2 : 3 : 4-*Trimethyl δ-Arabonolactone.*—This was prepared as described by Drew and Haworth (this vol., p. 778). The crystals (m. p. 45°), which were drained on porous tile in a vacuum, could not be recrystallised owing to the remarkable tendency of the

* This lactone has now been prepared from a different source and identified through the crystalline phenylhydrazide. This specimen gives rather higher mutarotation figures. The result is to increase slightly the declination of the curve for this lactone in Fig. 1, but its relative position in the sequence of the curves is not affected.

substance to absorb water (Found: C, 50·7; H, 7·3; OMe, 45·5. Calc. for $C_8H_{14}O_5$: C, 50·5; H, 7·4; OMe, 48·9%).

For the lactone in water ($c = 1·411$), the following values were observed:

Time (hrs.).	$[\alpha]^{20°}_{5461}$.	% Lactone present.	Time (hrs.).	$[\alpha]^{20°}_{5461}$.	% Lactone present.
0	+206°	100	2·0	+70°	28·4
0·07	199	96·3	2·5	45	15·3
0·5	161	76·3	3·2	21	2·6
1·4	104	46·3	3·8	17	0·5 (constant)

For the lactone: $[\alpha]^{21°}_{5461}$ +206·3°, $[\alpha]^{21°}_{3780}$ +183·5°, $[\alpha]^{21°}_{D}$ +179·5° in water ($c = 1·411$). For the acid (calculated as lactone): $[\alpha]^{19°}_{5461}$ +16° in water ($c = 0·72$), rising after 2 days to $[\alpha]^{21°}_{5461}$ +18° (compare Pryde, Hirst, and Humphreys, J., 1925, **127**, 355).

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CLXXI.—*The Nature of the Alternating Effect in Carbon Chains. Part XIX. The Mechanism of Certain Aromatic Migrations.*

By CHRISTOPHER KELK INGOLD, ERNEST WALTER SMITH, and CHARLES CYRIL NORREY VASS.

IN explanation of the process of halogenation, Fry, Cofman, Francis, and others have supposed that the halogen molecule ionises, the positive ion being the active agent. Whilst, however, it seems unlikely that such a decomposition, involving the exclusive appropriation of electrons by one atom, would take place without external excitation, the electron repulsion of a negative centre (*e.g.*, in an aromatic nucleus) might supply the necessary stimulus by tending to divest a halogen atom of its shared electrons during combination, leaving the other halogen atom to escape as a negative ion. Thus, the activity of a molecular chlorinating agent, X·Cl, should increase with the electron affinity of X, and similarly for bromination and iodination, which agrees with the fact that bromine chloride is a powerful brominating agent, but does not chlorinate, that iodine

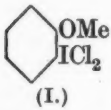
monochloride iodinates, and, generally, that the efficiency of halogenating agents is in the anticipated order (electron affinity sequence: Cl > Br > I > OH):

Cl·Cl > OH·Cl	Cl·Br > Br·Br > OH·Br	Cl·I > I·I
(chlorinating agents)	(brominating agents)	(iodinating agents)

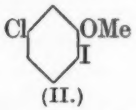
On the other hand, iodine trichloride is a chlorinating agent, but this is explicable on the theory of "singlet" linkings (Prideaux, *Chem. and Ind.*, 1923, **42**, 672; Ingold and Ingold, J., 1926, 1314; Sugden, this vol., p. 1174), since the *positively charged* iodine atom will attract electrons very strongly.

Reasoning on these lines, we deduced, for instance, that the "rearrangements" of aryl iodide dichlorides are not true internal migrations, but substitutions in one aromatic molecule of chlorine derived from another, the process being regenerative and continuous (compare Ingold and Ingold, *loc. cit.*). From this it follows that the ortho–para-migration law need not necessarily be obeyed, and that ordinary orientation rules should hold. A search of the literature revealed much that is consistent with this view [including the important observation by Brazier and McCombie that *p*-iodophenol dichloride, in which the *p*-position is blocked, yields 2-chloro-4-iodophenol (J., 1912, **101**, 968)], and nothing inconsistent with it, except the following.

o-Iodoanisole dichloride (I) was prepared by Jannasch and Hinterskirch (*Ber.*, 1898, **31**, 1710), who diagnosed the main product of its decomposition as 5-chloro-2-iodoanisole (II) (para-migration). According to the above mechanism, this would mean that iodine is more strongly *op*-orienting than methoxyl, which is contrary both to the theoretical sequence of these groups and to the order indicated by nitration experiments (Reverdin, *Ber.*, 1896, **29**, 997). The case, in fact, is one in which a meta-"migration" would be anticipated, and, actually, an independent synthesis (*vide* experimental portion) of 4-chloro-2-iodoanisole (III) has shown that this is the real structure of Jannasch and Hinterskirch's product.



(I.)



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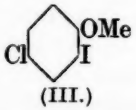

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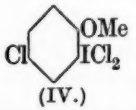
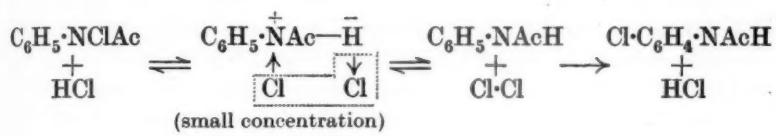


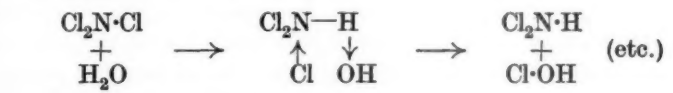
(IV.)

The group ·NHAc is more strongly *op*-orienting even than ·OMe (Ingold and Ingold, *loc. cit.*), and collateral evidence of the intermolecular character of these "migrations" was obtained by allowing the dichloride (IV) to decompose in the presence of acetanilide; the latter then acted as an acceptor for chlorine, the products being *p*-chloroacetanilide and chloroiodoanisole (III).

A somewhat similar transference of chlorine to a "foreign" aromatic nucleus has been established by Orton and King (J., 1911, **99**, 1185) for *N*-chloro-anilides in the presence of hydrogen chloride, which Armstrong (J., 1900, **77**, 1051) proved to be necessary for the conversion of the *N*-chloro-compounds into their *p*-chloro-isomerides. The corresponding explanation, which involves the addition of hydrogen chloride, through hydrogen, to the unshared nitrogen electrons,

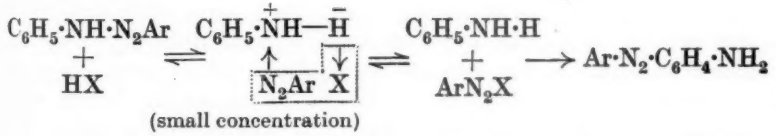


incorporates all the essential features of Orton's theory and one feature of Armstrong's (compare *Brit. Assoc. Reports*, 1910, 85), and is consistent with the equilibrium established by Orton and Jones (J., 1909, **95**, 1456) and with the available dynamical data (Blanksma, Orton). It corresponds closely with Sidgwick's explanation of the hydrolysis of halides in its application to nitrogen halides (J., 1924, **125**, 2672),



and shows how the lability of the halogen depends on the distribution of charges in the ammonium complex.

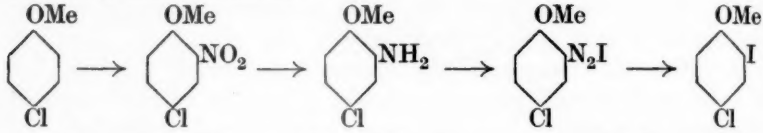
The "rearrangement" of aromatic diazoamino-compounds may be similarly regarded, the final irreversible reaction being a diazo-coupling:



This scheme is also in agreement with dynamical observations (Goldschmidt), and here again the transference of the ArN_2-group to a foreign nucleus has been realised (Nietzki, *Ber.*, 1877, **10**, 662). Other aromatic migrations may differ in certain respects from the above (see p. 1249), but a circumstance common to them all may be assumed to be the withdrawal of electrons from the mobile group by the attraction of a positively charged atom (compare Orton, *Proc. Roy. Soc.*, 1903, **71**, 156).

EXPERIMENTAL.

Preparation of 4-Chloro-2-iodoanisole.—This was obtained from *p*-chlorophenol as follows:



p-Chloroanisole (b. p. 194—198° uncorr.; recorded b. p. 198—202° corr.), obtained by methylation of *p*-chlorophenol with methyl sulphate and 10% sodium hydroxide, was nitrated with cooling and constant stirring in acetic anhydride solution, 5% more than the theoretical quantity of nitric acid (*d* 1·5), previously dissolved in the same solvent, being used. Water was added, and after decomposition of the acetic anhydride the nitro-compound was collected, and washed with dilute sodium hydroxide solution to remove the colour, and with water. The yield was 93% (m. p. 96—97·5°; recorded m. p. 97·5°). Reduction was effected by means of stannous chloride in hot hydrochloric acid, and the 4-chloro-*o*-anisidine (yield 95%, m. p. 82°) isolated by prolonged distillation in steam after addition of a large excess of concentrated sodium hydroxide solution. The base was diazotised in dilute hydrochloric acid below 5°, and the solution was treated with an excess of potassium iodide and warmed until the evolution of nitrogen ceased. The product was distilled in steam, the distillate extracted with ether, and the extract washed successively with hydrochloric acid, sodium hydroxide solution, and water. The residue obtained after drying and evaporation of the ether readily solidified, and crystallised from ligroin in large, transparent, rhomboidal plates, m. p. 48° (Found: C, 31·1; H, 2·1. C_7H_6OClI requires C, 31·3; H, 2·2%).

Chlorination of o-*Iodoanisole.*—Jannasch and Hinterskirch's *o*-iodoanisole dichloride was obtained without difficulty when a chloroform solution (50 c.c.) of *o*-iodoanisole (10 g.) was saturated with dry chlorine. A bright yellow solid separated, which was collected and washed with chloroform; it then melted at about 63° (decomp.). Hydrogen chloride was evolved in the cold, and the main product, contaminated with a pink oil, consisted of the characteristic rhomboidal plates, m. p. 48° (Found: C, 31·3; H. 2·1%), identical with those described above (mixed m. p. 48°).*

* In Beilstein's "Handbuch" (4te Aufl., Bd. VI, s. 209) the oil, b. p. 273—278°, described by Jannasch and Naphtali (*Ber.*, 1898, **31**, 1715) as the product of decomposition of *o*-iodophenetole dichloride, is referred to as "5-chloro-2-iodophenetole," evidently by analogy with Jannasch and Hinterskirch's "5-chloro-2-iodoanisole." The revision in the orientation of the latter involves a corresponding change in the formula of its homologue.

Dichlorination of o-Iodoanisole.—During an attempted preparation of *o*-iodoanisole dichloride, evolution of hydrogen chloride set in, and an iodo-dichloride was obtained probably identical with that described below. This in course of time decomposed, giving a green liquid, from which, by cooling, needles, m. p. 37°, of apparently a *dichloroiodoanisole* were obtained (Found: C, 27·9; H, 2·0. $C_7H_5OCl_2I$ requires C, 27·7; H, 1·65%).

Chlorination of 4-Chloro-2-iodoanisole.—The iodo-dichloride, which was prepared by means of chloroform in the usual way, has a deeper yellow colour than that derived from *o*-iodoanisole, and melts at about 76° (decomp.). The product of its spontaneous decomposition in chloroform solution was a brown oil, from which, by cooling, crystals of the compound, m. p. 37°, and of 4-chloro-2-iodoanisole (m. p. 48°) were obtained.

Chlorination of Acetanilide by an Aryl Iodide Dichloride.—The dichloride (4 g.) of 4-chloro-2-iodoanisole and acetanilide (1·4 g.) were together dissolved in chloroform. Heat was spontaneously generated, hydrogen chloride was evolved, and the yellow colour of the iodo-dichloride quickly disappeared. The product obtained on concentration of the chloroform solution was distilled in steam, and the residue crystallised from hot water; 1·4 g. (80%) of almost pure *p*-chloroacetanilide were then obtained (m. p. 171—174°; m. p. when fully purified, 175°). The distillate, which contained a liquid and a solid besides the aqueous layer, was filtered; the solid melted at about 60° and appeared to be impure *o*-chloroacetanilide. The non-aqueous liquid, which contained a little chloroform, when separated, dried, and left in a vacuum, completely solidified, yielding nearly pure 4-chloro-2-iodoanisole (m. p. 40—45° unpurified), which was identified, after purification, by direct comparison.

Other Rearrangements.—Numerous experiments, which need not be described in detail, have been made (and are being continued) in order to ascertain whether the hydroxyl group in β-arylhydroxylamines and the arylimino-group in αβ-diarylhydrazines can be transferred to a foreign nucleus by allowing the rearrangement with acids to occur in the presence of another strongly orienting aromatic compound (arylamines and their derivatives, and phenols in solutions of different hydrogen-ion concentration have been used); and whether migrations, directed by an independent substituent, to the meta-position of the same nucleus can be realised. The results have so far been wholly negative, and although we find it difficult entirely to convince ourselves on the grounds of such observations, the conclusion seems to be that the rearrangements of arylhydroxylamines and the benzidine and semidine conversions are not intermolecular processes in the same sense as are the reactions

discussed in the introduction to this paper. We are studying along similar lines the migration of nitroxyl and alkyl groups from a side chain to the aromatic nucleus.

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CLXXII.—*The Alleged Second Isoelectric Point of Gelatin.*

By BHUPENDRA NATH GHOSH.

THE observation of a minimum in the viscosity curve of gelatin at p_H 7·7 at 40° by Davis and Oakes (*J. Amer. Chem. Soc.*, 1922, **44**, 464) and of a similar minimum in swelling by Wilson and Kern (*ibid.*, p. 3633; 1923, **45**, 3139) led to the suggestion that gelatin has a second isoelectric point at this p_H. This was further supported by Matthews (*ibid.*, 1924, **46**, 852), who noticed two minima in the ultra-violet absorption spectrum of gelatin at p_H 4·7 and p_H 7·65, corresponding to the two isoelectric points. Wilson and Kern tried to explain these properties by assuming that gelatin can exist in two forms, the " gel " and the " sol " form, the former having an isoelectric point at p_H 4·7 and the latter at p_H 7·7. Increase of temperature or of p_H can transform the " gel " form to the " sol " form. Kraemer (*J. Physical Chem.*, 1925, **29**, 411) and Kraemer and Fanselow (*ibid.*, p. 1169) have further investigated the subject. They have discussed the different views regarding the existence of the two forms of gelatin, *i.e.*, the " sol " and " gel " forms of Wilson and Kern, and the keto-enol transformation suggested by Lloyd (*Biochem. J.*, 1920, **14**, 147), and have concluded that such assumptions are not justifiable and do not lead to useful results. They believe that the properties of gelatin can in many respects be explained from our knowledge of the behaviour of such colloids as ferric hydroxide sol. In Kraemer's opinion, the second isoelectric point at p_H 7·7 corresponds with the neutralisation of the negative charge of gelatin by positive ions in the alkaline solution.

Bogue (*J. Amer. Chem. Soc.*, 1925, **47**, 1194) has recently measured the optical rotation of gelatin sol at different hydrogen-ion concentrations, and concludes that gelatin has no second isoelectric point at p_H 7·7. In view of these controversies, it seemed desirable to measure the electrical charge of gelatin over a range of hydrogen-ion concentrations covering the two isoelectric points. The electro-endosmotic method of measurement has been chosen as being very suitable for measuring the charge of colloidal gels. Moreover, this method gives an idea of the resultant charge per unit area of the

surface, and hence, even if gelatin contains particles having opposite charges, then, assuming that the amount of charge carried by each particle is the same, the rate of flow of water gives an indication as to which type of particle is in excess.

Experimental.

The gelatin used was purified by repeated washing with dilute acetic acid solution as suggested by Loeb (*J. Gen. Physiol.*, 1918, **1**, 45). The purified sample was dehydrated by washing it with absolute alcohol and then dried in air. Its ash content was 0·23%. 1·5 G. of the substance were placed in a Pyrex glass bottle containing 300 c.c. of a dilute sodium hydroxide and phosphoric acid mixture at 20° and left in contact with the solution for 24 hours. The p_H of the solution in equilibrium with the substance was determined by comparison with a set of standards as recommended by Clark and Lubs. The swollen masses of gelatin were then transferred to a U-tube, melted by warming in a water-bath, and then allowed to set at 18° for nearly 4 hours. The U-tube was then filled with the solution with which the jelly had previously been left in contact. The other experimental arrangements were exactly the same as described by the author in a previous paper (J., 1926, 2609). The experiments were carried out at 18° and the results are given in Table I, in which *b* represents the distance (in cm.) moved by the air bubble in 3 minutes. The plus and minus signs in the *b* columns indicate the charge of the set gel.

Table I.

p_H.	*b*.	p_H.	*b*.	p_H.	*b*.
3·6	0·8(+)	6·0	0·6(−)	8·0	1·6 (−)
4·2	0·3(+)	6·6	0·9(−)	8·8	1·85(−)
4·8	0·0	7·0	1·2(−)		
5·2	0·2(−)	7·4	1·4(−)		

The above results show that gelatin has only one isoelectric point, in the neighbourhood of p_H 4·8. Below that it is positively charged and the charge increases as the p_H diminishes. Above p_H 4·8 the negative charge on the diaphragm increases with the rise in p_H within the range investigated. There is thus no indication of neutralisation of the negative charge of the substance at p_H 7·7. In view of the recent observations of Kruyt and Tendeloo (*J. Physical Chem.*, 1925, **29**, 1303), it might be thought that the multivalent phosphate ion had some influence on the negative charge of gelatin. Experiments were therefore performed using sodium hydroxide solution alone. The results are given in Table II; they, too, show no indication of an inversion in the electrokinetic potential of gelatin at p_H 7·7.

TABLE II.

p_H	7·0	7·6	8·6
b	1·0(−)	1·3(−)	1·7(−)

The above experiments also throw light on the structure of gelatin gels. There are different views regarding their structure: (1) Procter, Wilson, Katz, and others believe that gels form a sort of homogeneous solid solution; (2) Wo. Ostwald and others consider them to be two-phase liquid–liquid systems; (3) many others think that gels are two-phase solid–liquid systems and have an open network-like structure. Hatschek (Faraday Soc. Discussion, October, 1921) has shown that the mechanical properties of gels cannot be explained on the basis of the two-phase liquid–liquid theory of structure. In our experiments the occurrence of electro-endosmotic flow of water through a gelatin gel when it is used as the diaphragm material has been definitely established. This fact seems inexplicable on the solid-solution theory. It points to the conclusion that gelatin gel must have a porous capillary-like structure. The gelatin forms the solid walls of the capillaries and the pores are filled with the electrolyte solution. When an electric field is applied across a diaphragm of the gel, the liquid flows through the zig-zag system of capillaries. The above experiments therefore furnish strong evidence in favour of the third view of gel structure.

My best thanks are due to Prof. J. N. Mukherjee for his advice and encouragement.

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CLXXIII.—*The Influence of Groups and Associated Rings on the Stability of Certain Heterocyclic Systems. Part II. The Substituted Succinimides.*

By SARBBANI SAHAY GUHA SIRCAR.

IN Part I (this vol., p. 600) evidence was brought forward of the well-marked influence of substituents in modifying the stabilities of substituted glutarimides. The present work deals with the velocity of hydrolysis of the substituted succinimides, containing a five-membered ring. Table I, giving the velocity coefficients for these compounds calculated for a bimolecular reaction, clearly shows the close general agreement of the experimental results with the requirements of the modified strain theory. There are, however,

several other points of interest in the investigation. For example, the methyl group is found to produce an abnormal increase in the stability of the ring. This abnormality, although present in the glutarimide series, was masked by the unusually high value of the velocity coefficient for glutarimide itself. The anomalous behaviour of methyl in comparison with other alkyl groups is well known, particularly its influence on the dissociation constants of various series of acids (compare *Rec. trav. chim.*, 1912, **31**, 86; J., 1925, **127**, 342). A second point of interest is that the velocity coefficient for the first member of the series of succinimides is very nearly the same as the coefficients for the last two members. It seems as if the limit of stability of this system is reached in succinimide, or as if the *cyclo*pentane and the *cyclo*hexane rings are behaving like strainless systems, contributing little towards increasing the strain in the imide ring.

TABLE I.

Substituents.	$k \times 10^6$.
H,H	232
Me,H	141
Et,H	512
Me,Me	308
Me,Et	288
Et,Et	247
*cyclo*Pentane	235
*cyclo*Hexane	226

TABLE II.

Substance.	$k \times 10^6$.
Phthalimide	8,700
Homophthalimide	12,600
trans-Hexahydrophthalimide	26,500
trans-Hexahydrohomophthalimide	4,980
*trans-cyclo*Pentane-1-carboxy-2-acetimide	6,460

The study of a number of associated ring systems in which the hetero-ring is attached to the carbocyclic ring by two carbon atoms is not without interest. The velocity coefficients are in Table II. The associated systems seem to be less stable than the corresponding *spiro*-systems. This is a logical consequence of the strain theory if it is assumed that during the formation of the ring from the open chain the approximation of the ends of the chain (brought about by the influence of the substituents) may go beyond the requirement of closest spatial proximity; in other words, that the ends of the chain may overlap. In such a case the molecular strain would tend to increase rather than diminish as the effect of the substituent on the individual carbon atom becomes greater. It is also evident that the order of stability in passing from the five- to the six-membered ring may be reversed by this overlapping, making hexahydrohomophthalimide more stable than the lower homologue. In phthalimide and its homologue, however, the internally compensated (either by conjugation or by the mobility of the bonds) benzene nucleus prevents any rigid or permanent alteration in the extracyclic bonds, and the order of stability is the same as in the unsubstituted succinimide and glutarimide.

EXPERIMENTAL.

Preparation of the Imides.—All the imides were prepared by the method described in Part I (*loc. cit.*). Their structures were confirmed by regenerating the parent acids by hydrolysis with alkali.

Succinimide, m. p. 126° (Found: N, 14·4. Calc.: N, 14·1%). Methylsuccinimide, m. p. 66° (Found: N, 12·1. Calc.: N, 12·4%). Ethylsuccinimide, m. p. 77° (Found: N, 11·3. Calc.: N, 11·0%). *as*-Dimethylsuccinimide crystallised from hot water in scales, m. p. 106° (Found: N, 11·1. Calc.: N, 11·0%).

as-*Methylethylsuccinimide* was redistilled and then crystallised from acetone–ether; m. p. 64—65° (Found: N, 9·5. $C_7H_{11}O_2N$ requires N, 9·9%).

as-*Diethylsuccinimide.*—The acid was prepared by a slight modification of Higson and Thorpe's method (J., 1906, **89**, 1456) suggested by Dr. S. B. Dutt (private communication). A mixture of ethyl α-cyano-ββ-diethylacrylate (36 g.) (Birch and Kon, J., 1923, **123**, 2440), alcohol (400 c.c.), and potassium cyanide (15 g. in 30 c.c. of water) was kept for 2 weeks. The alcohol was then distilled off and the solution acidified. The heavy oil thus obtained could not be distilled in a vacuum without decomposition; so it was hydrolysed by boiling it with concentrated hydrochloric acid (5 vols.) for 10 hours under reflux. The material extracted from the cooled solution by ether was itself extracted with sodium carbonate solution, which was then filtered, acidified, saturated with ammonium sulphate, and repeatedly extracted with ether. The oily residue obtained on evaporation of the dried extracts soon solidified; it was then crystallised from dilute hydrochloric acid and again from benzene–petrol, the yield of the acid, m. p. 108°, being 20%. The *imide* crystallised from hot water in needles, m. p. 85—86° (Found: N, 9·5. $C_8H_{13}O_2N$ requires N, 9·0%).

cyclo*Pentane*spiro*succinimide* crystallised from water in plates, m. p. 124° (Found: N, 8·8. $C_8H_{11}O_2N$ requires N, 9·1%).

cyclo*Hexane*spiro*succinimide.*—The imide crystallised from hot water has m. p. 145° (Found: N, 8·25. $C_9H_{13}O_2N$ requires N, 8·3%).

Phthalimide, m. p. 229°. The velocity coefficient obtained by Miolati, *viz.*, 0·087, was utilised.

trans-*Hexahydrophthalimide.*—Hexahydrophthalic acids (*cis*- and *trans*-), prepared by Baeyer's method (*Annalen*, 1890, **258**, 145; 1892, **269**, 145), gave the same imide on distillation of the dry ammonium salts. This is regarded as the trans-*imide*, as it gives the *trans*-

acid on hydrolysis. It crystallised from hot water in large, glistening scales, m. p. 163—164° (Found: N, 9·4. $C_8H_{11}O_2N$ requires N, 9·2%).

Homophthalimide.—The acid, m. p. 173—174°, was prepared by reducing phthalonic acid with hydriodic acid and red phosphorus (*Ber.*, 1898, **31**, 369). The *imide* crystallised from hot water in scales, m. p. 75° (Found: N, 8·2. $C_9H_7O_2N$ requires N, 8·7%).

trans-*Hexahydrohomophthalimide.*—The acid (1-carboxy*cyclo*hexane-2-acetic acid) was prepared by Dutt's method (unpublished work), by condensing ethyl sodiocyanoacetate with ethyl Δ^1-tetrahydrobenzoate, and hydrolysing the resulting cyano-ester (b. p. 216°/20 mm.) by boiling it with concentrated hydrochloric acid (5 vols.) for 18 hours. (If the heating is less prolonged, a difficultly separable mixture of *cis*- and *trans*-acids is obtained.) The *trans*-acid thus formed (also described by Windaus, *Ber.*, 1923, **56**, 90) melted at 158° (Found: C, 58·1; H, 7·3. Calc.: C, 58·0; H, 7·6%). The *imide* crystallised from hot water in scales, m. p. 185° (Found: N, 8·0. $C_9H_{13}O_2N$ requires N, 8·4%).

trans-cyclo*Pentane*-1-*carboxy*-2-*acetimide* was prepared by a method similar to the previous one. *Ethyl* Δ^1-cyclo*pentenecarboxylate* was prepared by treating ethyl *cyclo*pentan-1-ol-1-carboxylate with phosphorus pentachloride and heating the product with diethylaniline (1·2 mols.) for 3 hours at 200°; it boiled at 92°/25 mm. and the yield was about 50% (Found: C, 68·3; H, 8·5. $C_8H_{12}O_2$ requires C, 68·5; H, 8·5%). The unsaturated ester (1 mol.) was treated with ethyl cyanoacetate (1 mol.) in presence of sodium ethoxide (1 mol.) dissolved in alcohol, and the mixture was heated on the steam-bath for 6 hours. The addition *compound* (yield 35%), which boiled at 185—186°/17 mm. (Found: C, 61·3; H, 7·4. $C_{13}H_{19}O_4N$ requires C, 61·6; H, 7·5%), was boiled with concentrated hydrochloric acid for 18 hours. The organic *acid* was extracted with ether and recrystallised thrice from dilute hydrochloric acid and then from benzene–petrol (b. p. 60—80°). It melted at 158°, was presumably the *trans*-acid, and behaved similarly to the *cyclo*hexane analogue (Found: C, 55·4; H, 7·1. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%). The *imide* crystallised from petrol–ether in scales, m. p. 184—185° (Found: N, 9·4. $C_8H_{11}O_2N$ requires N, 9·15%).

Hydrolysis of the Imides.—N/190-Solutions of the imides were hydrolysed in the manner described in Part I (*loc. cit.*, p. 602). The results are in Table III, the letters having the same significance as before. Where $a = 10$, N/200-acid was used in the titrations; where $a = 5$, N/100-acid was used. For small velocity coefficients, titrations were made at intervals of 10 minutes.

TABLE III.

Succinimide ($a = 10$).

t.	$a-x$.	$k \times 10^6$.
0	10·0	—
5	9·9	(202)
10	9·75	256
20	9·55	232
30	9·35	234
40	9·15	232
50	9·0	202
60	8·75	235
70	8·6	232
	Mean	232
(Miolati's value, 238)		

Methylsuccinimide ($a = 10$).

t.	$a-x$.	$k \times 10^6$.
0	10·0	—
10	9·85	152
20	9·75	128
30	9·6	139
40	9·5	132
50	9·4	127
60	9·15	153
70	9·0	157
80	8·8	(174)
100	8·5	(176)
	Mean	141
(Miolati's value, 135)		

Ethylsuccinimide ($a = 5$).

t.	$a-x$.	$k \times 10^6$.
0	4·85	—
5	4·8	(833)
10	4·75	526
15	4·6	550
20	4·55	494
25	4·45	494
30	4·35	498
	Mean	512

as-Dimethylsuccinimide ($a = 5$).

0	5·2?	—
5	5·0?	—
10	4·9	(204)
15	4·8	277
20	4·7	319
25	4·65	301
35	4·5	317
40	4·425	322
	Mean	308

as-Methylethylsuccinimide ($a = 10$).

0	10·0	—
10	9·7	309
20	9·45	264
30	9·25	270
40	8·95	307
50	8·75	285
60	8·5	293
	Mean	288

as-Diethylsuccinimide ($a = 10$).

0	10·0	—
5	9·8	(409)
10	9·75	256
20	9·5	263
30	9·35	231
40	9·1	247
50	8·9	247
60	8·7	241
	Mean	247

*cyclo*Pentane*spiro*-succinimide ($a = 5$).

0	—	—
5	4·95	(202)
10	4·85	(307)
15	4·80	263
20	4·775	233
25	4·725	232
35	4·6	248
	Mean	235

*cyclo*Hexane*spiro*-succinimide ($a = 5$).

0	5·0	—
5	4·95	(202)
10	4·85	(307)
15	4·80	263
20	4·75	232
25	4·725	217
35	4·65	215
46	4·55	—
	Mean	226

trans-Hexahydrophthalimide ($a = 5$).

0	4·5	Excess.
5	2·1	26,600
10	1·35	27,000
15	1·0	26,600
20	0·75	28,300
25	0·65	26,000
30	0·60	24,400
	Mean	26,500

Homophthalimide ($a = 5$).

0	3·7	—
5	2·8	(15,700)
10	2·25	12,700
15	1·75	12,300
20	1·4	12,800
25	1·15	12,700
30	1·05	12,500
35	0·90	13,000
	Mean	12,600

trans-Hexahydrohomophthalimide ($a = 5$).

0	4·75	—
5	4·05	4690
10	3·5	4300
15	3·05	4260
20	2·4	5410
25	2·15	5300
32	1·8	5500
39	1·4	5400
	Mean	4980

trans-cyclo-Pentane-1-carboxy-2-acetimide ($a = 5$).

0	4·3	—
5	3·8	6310
10	3·1	6130
15	2·5	6160
20	2·15	6130
25	1·8	7100
30	1·6	7080
35	1·4	6320
	Mean	6460

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CLXXIV.—*The Influence of Groups and Associated Rings on the Stability of Certain Heterocyclic Systems. Part III. The Substituted Paraconic Acids.*

By Sarbbani Sahay Guha Sircar.

The stability of five- and six-membered heterocyclic systems containing nitrogen having been examined (this vol., pp. 600 1252), a study has been made of five-membered rings containing oxygen. For this purpose the substituted paraconic acids were suitable. Three disubstituted acids had already been prepared by Birch, Gough, and Kon (J., 1921, **119**, 1320), and two others (methylethyl and *cyclo*pentane compounds) were obtained from the corresponding ketones by their method. The monosubstituted paraconic acids were prepared by Fittig's well-known method.

As paraconic acid and its monoalkyl derivatives can be neutralised at the ordinary temperature without fission of the lactone ring, which is only attacked by hot alkali (Fittig, *Ber.*, 1890, **23**, 91), it was possible in the present investigation to use two equivalents of alkali, one to neutralise the acid and the other to effect the opening of the ring; the first process, being instantaneous, had no undesirable effect on the hydrolysis. At 25° the velocity of hydrolysis was conveniently rapid in the solution prepared by adding 10 c.c. of $N/10$-sodium hydroxide to 90 c.c. of an $N/180$-solution of a paraconic acid.

The results of the hydrolyses given in Table I again show strikingly the influence of substituents on the stability of a heterocyclic system. The introduction of a methyl group causes, as was also observed in the two previous investigations, an increase in the stability. The influence of two ethyl groups is, however, greater than that of the *cyclo*pentane or *cyclo*hexane group.

Table I.

Substituents.	$k \times 10^5$.	Substituents.	$k \times 10^5$.
H, H	1630	Me, Et	164
Me, H	763	Et, Et	74·5
Et, H	652	*cyclo*Pentane	119
Me, Me	270	*cyclo*Hexane	107

Experimental.

Paraconic acid was prepared by decomposing itabromopyrotartaric acid by water (*Annalen*, 1882, **216**, 77; in the preparation of itabromopyrotartaric acid by the addition of hydrobromic acid to itaconic acid it was found convenient to heat the mixture at

100° for 3 hours) and purified by means of the silver salt. The acid was very hygroscopic; m. p. 57° (Found: C, 45·8; H, 5·0. Calc.: C, 46·15; H, 4·6%). Methylparaconic acid (Fittig, *Ber.*, 1890, **23**, 91) was slightly hygroscopic; m. p. 84·5° (Found: C, 49·8; H, 5·8. Calc.: C, 50·0; H, 5·55%). Ethylparaconic acid (Fittig, *loc. cit.*) had m. p. 85° (Found: C, 53·0; H, 6·6. Calc.: C, 53·2; H, 6·3%). Dimethylparaconic acid (terebic acid) (Birch, Gough, and Kon, *loc. cit.*) crystallised from water in scales, m. p. 174° (Found: C, 53·4; H, 6·4. Calc.: C, 53·1; H, 6·4%). Diethylparaconic acid (Birch and Thorpe, J., 1922, **121**, 1825) had m. p. 105° (Found: C, 57·85; H, 7·4. Calc.: C, 58·05; H, 7·5%). *cyclo*Hexane*spiro*paraconic acid (Birch, Gough, and Kon, *loc. cit.*) had m. p. 184—185° (Found: C, 60·3; H, 7·4. Calc.: C, 60·6; H, 7·1%).

Methylethylparaconic Acid.—This acid was prepared by a method similar to that employed in preparing the dimethyl compound (above). Details are not given, as they differed only in minor points from those recorded by Birch, Gough, and Kon. The *imide*, $CMeEt<\begin{matrix}C(CN)\cdot CO\\C(CN)\cdot CO\end{matrix}>NH$, was crystallised from alcohol; m. p. 225—227° (Found: N, 20·4. $C_{10}H_9O_2N_3$ requires N, 20·7%). 2 : 3-*Dicyano*-1-*methyl*-1-*ethyl*cyclo*propane*-2-*carboxylamide* crystallised from benzene in needles, m. p. 127—128° (Found: N, 23·4. $C_9H_{11}ON_3$ requires N, 23·7%). The *γ-lactone* of β-*hydroxy*-β-*ethylbutane*-γδδ-*tricarboxylic acid* crystallised from water on the addition of hydrochloric acid, m. p. 157—158° (efferv.) (Found: C, 49·7; H, 5·6. $C_9H_{12}O_6$ requires C, 50·0; H, 5·55%). *Methylethylparaconic acid* crystallised from hot water in needles, m. p. 131—132° (Found: C, 55·45; H, 6·7. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%. Found for the *silver* salt: Ag, 38·4. $C_8H_{11}O_4Ag$ requires Ag, 38·7%).

cyclo*Pentane*spiro*paraconic Acid.*—The preparation was similar to that of the *cyclo*hexane analogue (above). The bridged *imide* was crystallised from alcohol; m. p. 202—203° (Found: N, 20·3. $C_{11}H_9O_2N_3$ requires N, 20·9%). cyclo*Pentane*spiro-2 : 3-*dicyano*-cyclo*propane*-2-*carboxylamide* was crystallised from dilute alcohol; m. p. 126° (Found: N, 21·8. $C_{10}H_{11}ON_3$ requires N, 22·2%). The *γ-lactone* of 1-*hydroxy*cyclo*pentylethane*-αββ-*tricarboxylic acid* slowly crystallised from a small quantity of water after the addition of hydrochloric acid; m. p. 175—177° (efferv.). cyclo*Pentane*-spiro*paraconic acid* was prepared by heating the tribasic acid at 200° for 2 hours until the evolution of carbon dioxide ceased; it crystallised from water in needles, m. p. 127° (Found: C, 58·3; H, 6·4. $C_9H_{12}O_4$ requires C, 58·7; H, 6·5%. Found for the *silver* salt: Ag, 37·4. $C_9H_{11}O_4Ag$ requires Ag, 37·1%).

Details of the hydrolyses are recorded in Table II. $a = 5$ in all cases. (For the meaning of the letters, see preceding paper.)

TABLE II.

	Paraconic acid.		Methylparaconic acid.		Ethylparaconic acid.		Dimethylparaconic acid.	
t.	$a-x$.	$k \times 10^5$.	$a-x$.	$k \times 10^5$.	$a-x$.	$k \times 10^5$.	$a-x$.	$k \times 10^5$.
0	3·1	—	4·7	—	4·2	—	5·0	—
5	2·8	1430	3·7*	(878)	3·3	(857)	4·4	272
10	1·75	1850	2·8	788	2·75	743	3·9	266
15	1·35	1800	2·3	780	2·35	704	3·55	272
20	1·15	1670	2·0	750	2·2	606	3·2	271
25	1·0	1600	1·8	761	1·9	629	3·0	266
30	0·9	1510	1·55	772	1·65†	601	2·8	252
35	0·8	1560	1·35	730	1·5‡	630	2·5	285
	Mean	1630	Mean	763	Mean	652	Mean	270

	Methylethylparaconic acid.		Diethylparaconic acid.		*cyclo*Pentane-*spiro*paraconic acid.		*cyclo*Hexane-*spiro*paraconic acid.	
0	4·8	—	5·0	—	4·95	—	5·2	—
5	4·6	174	4·9	(41)	4·6	(174)	4·95	(202)
10	4·3	162	4·7	64	4·45	124	4·5	111
15	4·05	155	4·5	74	4·2	127	4·35	100
20	3·8	163	4·35	75	4·0	125	4·1	102
25	3·55	171	4·2	76	3·9	113	3·9	112
30	3·3	163	4·05	78	3·7	117	3·75	111
35	3·15	168	3·95	76	3·6	111	3·6	155
40	—	—	3·8	79	—	—	—	—
	Mean	164	Mean	74·5	Mean	119	Mean	107

*, †, ‡ values for 4, 31, and 37 minutes, respectively.

The author wishes to express his grateful thanks to Professor J. F. Thorpe, C.B.E., F.R.S., for his kind interest in the work and to the Chemical Society for a grant that partly defrayed the cost.

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CLXXV.—*Researches on Residual Affinity and Co-ordination. Part XXIX. Cupric Salts Stabilised by Ethylenediamine.*

By GILBERT T. MORGAN and FRANCIS HEREWARD BURSTALL.

ALTHOUGH cupric salts of the more strongly electronegative anions are stable exothermic compounds, this condition of stability depends largely on the nature of the acidic ions, and as their electronegative character diminishes, the normal cupric salts exhibit an increasing tendency to decompose either by hydrolytic change or by a spontaneous decrease of valency from bivalent to univalent copper.

The former mode of decomposition is exhibited by cupric carbonate, the latter by cupric iodide ($CuI_2 = CuI + I + 11{,}560$ cals.).

In earlier experiments on this subject (J., 1926, 2018, 2027) it was shown that cupric iodide can be stabilised by combination with ethylenediamine, and accordingly we have employed this new reagent $[Cu,2\,en,2H_2O]I_2$ in a further study of cupric salts of the weaker acids.

Amminated Cupric Carbonates.—The normal salt, $CuCO_3$, has not hitherto been obtained, since both laboratory methods and geological processes lead to the formation of basic carbonates. A double carbonate of normal type, $K_2[Cu(CO_3)_2]$, was obtained in anhydrous and hydrated forms by Reynolds (J., 1898, **73**, 262), but this substance is readily decomposed by water. A compound having the composition $CuO,3CO_2,4NH_3$ is described by Maumené (*Compt. rend.*, 1882, **95**, 225), and the diamminocupric carbonate, $CuCO_3,2NH_3$, by Favre (*Ann. Chim. Phys.*, 1844, **10**, 116). With the reagents cooled to − 18°, Ephraim isolated pentamminocupric carbonate, $CuCO_3,5NH_3$, which at 37° dissociated into the diammine (*Ber.*, 1919, **52**, 940).

By interaction between silver carbonate and aqueous bisethylenediamminocupric iodide we have now obtained *bisaquobisethylenediamminocupric carbonate*, $[Cu,2\,en]CO_3,2H_2O$, as a well-defined salt, readily soluble in water or alcohol to solutions which can be boiled without decomposition of the product.

Amminated Cupric Nitrites.—Cupric nitrite has not been obtained in a stable form, for when it is prepared in aqueous media, complex changes occur and nitric oxide is evolved at the ordinary temperature. A basic salt, $Cu(NO_2)_2,3Cu(OH)_2$, has been isolated (van der Meulen, *Ber.*, 1879, **12**, 758) and double nitrites such as $K_3[Cu(NO_2)_5]$ and $Tl_3[Cu(NO_2)_5]$ have been described (Kurtenacker, *Z. anorg. Chem.*, 1913, **82**, 204; Cuttica and Paciello, *Gazzetta*, 1922, **52**, i, 141). An amminated compound formerly described by Péligot (*Compt. rend.*, 1861, **53**, 209) as hydrated diamminocupric nitrite has since been proved by Bassett and Durrant to be anhydrous tetramminocupric nitrite,* $[Cu,4NH_3](NO_2)_2$, which at 97° dissociates into the anhydrous diammine $Cu(NH_3)_2(NO_2)_2$ (J., 1922, **121**, 2636).

Interaction between silver nitrite and diaquobisethylenediamminocupric iodide leads to *bisethylenediamminocupric nitrite*, an an-

* In Hoffmann's "Lexikon" and Gmelin-Kraut's "Handbuch der anorganischen Chemie," [VII], V, i, pp. 1569, 1123, 1576, 1578, references are given to the preparation by Pudschies of tetramminocupric nitrite, sulphite, and thiosulphate, but we have not been able to obtain the original publication (*Dissert.*, Strassburg, 1904).

hydrous, well-defined salt stable up to 120° and in boiling aqueous or alcoholic solutions.

Evidence was also gained of the existence of a similar complex cupric hyponitrite, although the compound was not isolated in a state of purity. A more decisive result was, however, obtained with cupric hypophosphite.

Bisethylenediamminocupric hypophosphite, $[Cu,2\ en](H_2PO_2)_2$, is stable up to 115° and in aqueous or alcoholic solution. The reducing action of the hypophosphite ion on bivalent copper is far less noticeable than with cupric hypophosphite, which furnishes copper hydride.

Amminated Cupric Sulphites.—The normal salt, $CuSO_3$, has not been isolated with certainty, and the causes of its instability are similar to those inducing the decomposition of cupric nitrite. Reduction of the cupric ion by the sulphite radical leads to the formation of cuprous compounds and the precipitation of sparingly soluble, red cupric cuprososulphite, $Cu(CuSO_3)_2,2H_2O$.

The stability of cupric sulphite is enhanced by ammination, for the tetrammine, $[Cu,4NH_3]SO_3,2H_2O$, is recorded by Pudschies (*loc. cit.*).

We have now obtained two ethylenediamine derivatives of normal cupric sulphite: *Monoaquoethylenediamminocupric sulphite*, $[Cu,en,H_2O]SO_3$, by the action of aqueous ethylenediamine on cupric cuprososulphite, and *bisethylenediamminocupric sulphite*, $[Cu,2\ en]SO_3$, by adding copper to a suspension of silver sulphite in ethylenediamine. The latter method is of general application in the preparation of amminated cupric salts.

The chemical properties of the foregoing complex cupric sulphites indicate clearly that the more fully co-ordinated compound, $[Cu,2\ en]SO_3$, is much the more stable of the two.

Amminated Cupric Thiosulphates.—A reducing action of the cupric ion occurs in interactions between soluble cupric salts and alkali thiosulphates, so that normal cupric thiosulphate has not hitherto been isolated. Amminated derivatives have, however, been recorded. Pudschies (*loc. cit.*) cites the tetrammine, $[Cu,4NH_3]S_2O_3$, and a more complex binuclear salt, $[Cu_2,3\ en,2H_2O](S_2O_3)_2$, is described by Benrath (*Z. anorg. Chem.*, 1917, **99**, 5).

Bisethylenediamminocupric thiosulphate, $[Cu,2\ en]S_2O_3$, which is stable up to 130°, is prepared by double decomposition between barium thiosulphate and bisethylenediamminocupric sulphate.

Amminated Cupric Polythionates.—Cupric dithionate crystallising with 4 or 5 molecules of water has long been known (Heeren, *Pogg. Annalen*, 1826, **7**, 181; Grailich and Murmann, *Ber. Wien. Akad.*, 1857, **27**, 171); it decomposes readily to a basic salt,

$[Cu,3Cu(OH)_2]S_2O_6$, of the atacamite type (compare the basic nitrite, p. 1260).

Two amminated derivatives of cupric dithionate are described: the tetrammine, $[Cu,4NH_3]S_2O_6$ (Heeren, *loc. cit.*; Schweitzer, *J. pr. Chem.*, 1856, **67**, 430; Horn, *Amer. Chem. J.*, 1908, **39**, 212), and the monoammine, obtained by the last-mentioned investigator from the tetrammine and liquid ammonia.

Bisethylenediamminocupric dithionate, $[Cu,2\ en]S_2O_6$, is a well-defined, sparingly soluble salt remaining undecomposed up to 280°. When trithionates and cupric salts interact in warm aqueous solution, copper sulphide is precipitated. Ammonia derivatives of cupric trithionate are not recorded, but stabilisation of this salt has now been obtained by the isolation of *bisethylenediamminocupric trithionate*, $[Cu,2\ en]S_3O_6$, stable up to 170°.

Cupric tetrathionate has been prepared by adding copper carbonate to Wackenroder's solution (Curtis and Hinkel, *J. pr. Chem.*, 1888, **37**, 148), but the only amminated derivative on record is the tetrapyridine compound $[Cu,4Py]S_4O_6$ (Calzolari, *Atti R. Accad. Lincei*, 1915, **24**, i, 921).

Bisethylenediamminocupric tetrathionate, $[Cu,2\ en]S_4O_6$, is a well-defined salt stable up to 160°.

The foregoing complex cupric polythionates which have the same general formula $[Cu,2\ en]S_xO_6$ exhibit a well-marked gradation of physical and chemical properties. As the sulphur accumulates in the molecule, the colour of the salt deepens, its solubility in water increases, and its decomposition temperature decreases.

Owing to the destructive action of ethylenediamine on alkali pentathionates from Wackenroder's solution, the complex cupric pentathionate of this series was not isolated. Other attempts made to complete the series of ethylenediamminocupric salts of sulphur oxy-acids were unsuccessful as regards hydrosulphurous acid, $H_2S_2O_4$, and formaldehydesulphoxylic acid, $CH(OH)HSO_2$, but the corresponding salt of persulphuric acid was isolated.

Amminated Cupric Persulphates.—Cupric persulphate has not been isolated, but its tetrammino- and tetrapyridine-derivatives, $[Cu,4\ base]S_2O_8$, have been prepared (Barbieri and Calzolari, *Z. anorg. Chem.*, 1911, **71**, 347).

Bisethylenediamminocupric persulphate, $[Cu,2\ en]S_2O_8$, is a sparingly soluble salt comparable in its explosive properties with ethylenediamminocupric perchlorate (J., 1926, 2026).

Bisethylenediamminocupric selenocyanate, $[Cu,2\ en](CNSe)_2$, furnishes a noteworthy example of the stabilising effect of ethylenediamine on a very decomposable cupric salt. Interaction of soluble selenocyanates and cupric salts leads to the precipitation of copper

selenide, both cupric and cuprous selenocyanates being unstable under these conditions. When, however, ethylenediamine is present, the separation of copper selenide is inhibited, and the complex salt, $Cu(CNSe)_2$,2 en, is obtained in stable, well-defined, anhydrous crystals.

Co-ordination Numbers of Bivalent Copper.

Of the eleven complex cupric salts described in this communication, ten contain two molecular proportions of ethylenediamine to one atomic proportion of copper, and of these ten salts, nine are anhydrous and include no other addenda than the diamine. Of the two anomalous salts, the sulphite [Cu, en, H_2O]SO_3 may be regarded as co-ordinatively unsaturated, whereas the dihydrated carbonate, $CuCO_3$,2 en,2H_2O, is of ambiguous character, with a co-ordination number for copper ranging from 4 to 6, according to the allocation of the two molecules of water between kation and anion.

In the other nine cases of anhydrous salts having the general formulæ [Cu,2 en]X_2' and [Cu,2 en]X'' (X' and X'' being monobasic and dibasic anions), the experimental evidence points to a co-ordination value of 4 for bivalent copper as being the predominant type most conducive to molecular stability.

From the wide range of derivatives examined, it is obvious that the stability of this fourfold co-ordination is not appreciably influenced either by the chemical nature or by the valency of the anion. The recurrence of the co-ordination complex with two implicated ethylenediamine molecules suggests the influence of forces making for symmetrical orientation of the two chelate groups. The discovery by Mills and Gotts of optical activity among copper compounds having a co-ordination number of 4 (J., 1926, 3124) affords direct proof of tetrahedral arrangement of the four associating units round the central copper atom. It is accordingly highly probable that in the bisethylenediamminocupric salts described below, a tetrahedral arrangement of the two chelate diamine groups is also present.

Regarded from the electronic point of view, the co-ordination complex [Cu,2 en]$''$ is still unsaturated, since the bivalent cupric ion with electronic structure 2,224,22445 (Main Smith, *J. Soc. Chem. Ind.*, 1924, **43**, 323) shares eight additional electrons with the two ethylenediamines, thereby giving to the co-ordinated atom the electronic structure 2,224,22445,224, which differs from the arrangement 2,224,22446,224 for krypton, the next inert gas, in a shortage of one electron in the ninth sub-group. Any addendum supplying one additional electron would complete the inert-gas structure with a co-ordination number of 5.

As, however, many 6-co-ordinated cupric complexes are also known, it is evident either that an electronic structure with three electrons in excess of krypton is possible, or, alternatively, that certain of the six associating units are contributing only one electron each, instead of the two which are generally regarded as operative in a non-polar linking.

It seems evident from a general survey of co-ordinated copper compounds that the forces making for symmetrical arrangement (co-ordination numbers 4 and 6) prevail over forces tending to reproduce the electronic structure of an inert gas. The co-ordination number 4 offers, in the case of the cupric ion, the optimum condition as regards symmetrical arrangement of associating units, coupled with a very close approximation to the saturated electronic structure of krypton.

EXPERIMENTAL.

Bisaquobisethylenediamminocupric Carbonate, $[Cu,2\,en]CO_3,2H_2O$. —A concentrated aqueous solution of hydrated bisethylenediamminocupric iodide, $[Cu,2\,en,2H_2O]I_2$, was triturated with a slight excess of freshly prepared silver carbonate. The purple filtrate was treated with alcohol–ether; the complex carbonate was then precipitated. Recrystallised from water after the addition of alcohol and ether, this salt separated as a very hygroscopic, purple, crystalline powder, m. p. 135° (decomp.), readily soluble in water or alcohol (Found in material dried over sulphuric acid: C, 21·2; H, 7·3; N, 19·8; Cu, 23·1. $C_5H_{20}O_5N_4Cu$ requires C, 21·45; H, 7·2; N, 20·0; Cu, 22·7%).

Aqueous or alcoholic solutions of this complex normal carbonate could be boiled without decomposition and were stable in the presence of caustic alkali, but were decomposed by dilute acids. Silver nitrate produced in them an immediate precipitation of silver carbonate even in the cold, thus indicating the ionised condition of the dissolved complex salt.

Bisethylenediamminocupric nitrite, $[Cu,2\,en](NO_2)_2$, was prepared by triturating together bisaquobisethylenediamminocupric iodide and freshly prepared silver nitrite (in slight excess); the filtrate from silver iodide was concentrated to a small bulk and left over sulphuric acid. The complex *nitrite* crystallised slowly from the syrupy solution in dark purple needles, which were purified by recrystallisation from water or alcohol, and also by reprecipitation from aqueous solution with ether and alcohol. After drying over sulphuric acid in a vacuum desiccator, the complex salt was anhydrous (Found: C, 17·9; H, 5·95; N, 29·9; Cu, 23·2; NO_2, 33·3. $C_4H_{16}O_4N_6Cu$ requires C, 17·4; H, 5·85; N, 30·5; Cu, 23·05; NO_2, 33·4%).

This complex nitrite, which melted with rapid decomposition at 128°, was extremely soluble in water, but less soluble in alcohol. In aqueous or alcoholic solution the salt was not decomposed even on boiling; caustic alkalis had no effect, but dilute acid caused immediate evolution of nitrous fumes. Silver nitrate produced a quantitative separation of silver nitrite in alcoholic solution, showing that the dissolved complex nitrite was ionised in this medium.

Attempted Preparation of an Ethylenediamminocupric Hyponitrite.—The replacement method (see p. 1266) employed in the case of the complex sulphite [Cu,2 en][SO_3] was tried with silver hyponitrite and metallic copper in the presence of ethylenediamine. Silver was deposited, and the resulting dark purple solution of complex cupric salts was concentrated to the crystallising point; purplish-blue plates were then obtained which had the composition of a complex cupric hyponitrite, [Cu,3 en][N_2O_2], mixed with the carbonate [Cu,2 en][CO_3,2H_2O], the latter being produced by absorption of carbon dioxide from the atmosphere. The impure salt dissolved readily in water, and on addition of silver nitrate the solution gave yellow silver hyponitrite.

Bisethylenediamminocupric Hypophosphite, [Cu,2 en](H_2PO_2)$_2$.—An aqueous solution of barium hypophosphite (5·3 g.) was added to one of copper sulphate (5·0 g.) containing ethylenediamine (2·4 g.), and the mixture shaken for some hours. After filtration from barium sulphate, the purplish-blue liquid was concentrated on the water-bath and left over concentrated sulphuric acid. The surface of the liquid soon became covered with a pale mauve, crystalline crust of hypophosphite, which was recrystallised from water and dried over sulphuric acid (Found: C, 15·7; H, 6·9; N, 17·9; P, 19·5; Cu, 20·5. $C_4H_{20}O_4N_4P_2Cu$ requires C, 15·3; H, 6·4; N, 17·85; P, 19·8; Cu, 20·3%).

Although this complex hypophosphite was hygroscopic, it remained unchanged when kept quite dry. On heating, the dry salt decomposed rapidly at 115—118° to a dark brown solid. It dissolved readily in alcohol; this solution was slowly decomposed in presence of sodium hydroxide, although the aqueous solution was unaffected. Hydrochloric and sulphuric acids caused decolorisation of the solution, and the latter acid gave a reddish precipitate of metallic copper. Silver nitrate solution gave a white precipitate in the cold, which darkened rapidly, with the separation of black metallic silver; in acid solution a silver mirror was obtained.

Bisethylenediamminocupric persulphate, [Cu,2 en]S_2O_8, was deposited in purplish-red, acicular crystals when aqueous potassium persulphate was added to an aqueous solution of copper sulphate

(1 mol.) containing ethylenediamine (2 mols.). The crystals were washed successively with cold water, alcohol, and dry ether and analysed immediately (Found: Cu, 16·8; S_2O_8, 51·0. $C_4H_{16}O_8N_4S_2Cu$ requires Cu, 16·9; S_2O_8, 51·15%).

The complex persulphate was extremely unstable, and when left in air or in the desiccator it decomposed, leaving a blue residue; one preparation exploded when contained in a cooled specimen tube. The salt detonated on percussion and exploded on heating or on warming with concentrated sulphuric acid.

Although only very sparingly soluble in cold water, the persulphate dissolved more readily on warming; the purple solution, which changed to blue without appreciable evolution of gas, yielded with barium salts a copious precipitate of barium sulphate. Silver nitrate gave no reaction in the cold, but, on warming, oxygen was evolved and the purple solution changed to blue. Concentrated hydrochloric acid caused decomposition with evolution of chlorine.

Monoaquoethylenediamminocupric Sulphite, $[Cu, en, H_2O]SO_3$.—The dark red cupric cuprososulphite prepared by warming a 20% solution of cupric sulphate with concentrated aqueous potassium bisulphite was shaken with a cold aqueous solution of ethylenediamine; a deep purple liquid was then obtained with deposition of copper. On addition of a considerable volume of alcohol to the filtered solution, the complex cupric sulphite separated in pale reddish-mauve nodules. The product was purified by solution in water and reprecipitation with alcohol. After drying over sulphuric acid, the salt was monohydrated (Found: C, 11·1; H, 5·0; N, 13·3; SO_3, 35·6; Cu, 28·5. $C_2H_{10}O_4N_2SCu$ requires C, 10·9; H, 4·5; N, 12·6; SO_3, 36·1; Cu, 28·7%).

The aqueous solution of the complex sulphite decomposed on warming to give a brown precipitate containing cuprous oxide; dilute sulphuric acid caused a separation of red metallic copper, whereas hydrochloric acid gave cuprous chloride, both reactions being accompanied by evolution of sulphur dioxide. On exposure to air this sulphite oxidised slowly; at 100° it blackened, and at higher temperatures its colour changed to brown.

Bisethylenediamminocupric Sulphite, $[Cu, 2\,en]SO_3$.—Metallic copper (2·5 g.) was added with constant stirring to a mixture of freshly prepared silver sulphite (11·8 g.), ethylenediamine (4·8 g.), and 50 c.c. of cold water. After being shaken for an hour, the mixture was filtered from metallic silver and the deep purple filtrate was evaporated to the crystallising point over sulphuric acid. Prismatic crystals of the complex sulphite slowly separated and the surface of the liquid became covered with a pale mauve crust of the salt. Recrystallisation from cold water and desiccation

over sulphuric acid gave well-defined, mauve, opaque, tabular and pyramidal crystals with matt surfaces. This anhydrous sulphite decomposed without melting at 190—200° (Found: C, 18·4; H, 6·2; N, 20·9; S, 12·2; Cu, 24·2. $C_4H_{16}O_3N_4SCu$ requires C, 18·2; H, 6·1; N, 21·25; S, 12·15; Cu, 24·1%).

Although hygroscopic, the complex sulphite remained unchanged in a closed vessel; its aqueous solution was not visibly affected by boiling. In cold solutions of the salt, silver nitrate, and barium chloride produced, respectively, copious white precipitates of silver and barium sulphites. With sodium hydroxide the solution remained clear, but its colour changed from purple to blue; the colour was discharged by mineral acids.

Bisethylenediamminocupric Thiosulphate, $[Cu,2\ en]S_2O_3$.—An aqueous solution of cupric sulphate (5·0 g.) containing 2·4 g. of ethylenediamine was triturated with excess of barium thiosulphate (6·0 g.), and the mixture shaken for several hours. The purplish-blue filtrate was then concentrated and cooled; the blue plates of the complex cupric thiosulphate that separated were crystallised from water containing a few drops of ethylenediamine (Found: C, 16·0; H, 5·6; N, 18·75; S, 21·5; Cu, 21·2. $C_4H_{16}O_3N_4S_2Cu$ requires C, 16·2; H, 5·45; N, 18·9; S, 21·7; Cu, 21·5%).

The complex thiosulphate remained unchanged in air, but on heating it decomposed without melting at 150—155°. The stable purplish-blue solution in water became blue on addition of aqueous sodium hydroxide, whereas warm alcoholic soda precipitated cupric oxide. Silver nitrate gave a white precipitate, blackening rapidly even in the cold. Sulphuric and hydrochloric acids discharged the purplish-blue colour of the solution, in the former case with the formation of a brown precipitate.

Bisethylenediamminocupric Dithionate, $[Cu,2\ en]S_2O_6$. — When 4·8 g. of sodium dithionate, 5·0 g. of copper sulphate, and 2·4 g. of ethylenediamine were mixed together in aqueous solution, a purplish-red, crystalline precipitate separated which became anhydrous after drying over sulphuric acid (Found: C, 13·45; H, 4·9; N, 16·0; S, 18·2; Cu, 19·1. $C_4H_{16}O_6N_4S_2Cu$ requires C, 14·0; H, 4·7; N, 16·3; S, 18·65; Cu, 18·5%).

This complex cupric dithionate was quite stable in air at the ordinary temperature, and on heating it decomposed with blackening at 260°. It was only very sparingly soluble in cold water, but dissolved more readily on warming to a stable purple solution. Barium chloride and silver nitrate were without action on the hot or cold solution; with sodium hydroxide the colour was changed to blue, whereas with mineral acids it was discharged.

Bisethylenediamminocupric Trithionate, $[Cu,2\ en]S_3O_6$.—A cold

aqueous solution of sodium trithionate (7·1 g.) was added to a cold solution of cupric acetate (5·9 g.) containing ethylenediamine (3·6 g.). The purple solution was filtered and an excess of alcohol added; the complex *trithionate* then separated in purple, matted needles. After recrystallisation from luke-warm water and desiccation over sulphuric acid, the trithionate was anhydrous (Found: C, 12·7; H, 4·5; N, 15·1; S, 25·9; Cu, 17·1. $C_4H_{16}O_6N_4S_3Cu$ requires C, 12·8; H, 4·3; N, 14·9; S, 25·6; Cu, 16·9%).

This salt was quite stable in the air under normal conditions, but on heating it decomposed without melting at 170—175°. Silver nitrate gave, in the cold, a white precipitate, rapidly becoming yellow and finally black; this decomposition was greatly facilitated by warming. Barium chloride had no action in the cold, but on heating a white precipitate was formed. Sodium hydroxide caused the purple aqueous solution to become blue, whereas dilute acids discharged the intense colour with deposition of copper sulphide.

Bisethylenediamminocupric Tetrathionate, $[Cu,2\ en]S_4O_6$.—An aqueous solution of 3·4 g. of cupric chloride, 2·4 g. of ethylenediamine, and 6·0 g. of sodium tetrathionate was cautiously concentrated and cooled; the large, deep purple, rhomboidal prisms that separated were crystallised from water. The original deposition of complex tetrathionate was preferably induced by the addition of alcohol to the original solution, thus obviating evaporation. When dried over calcium chloride, the salt was anhydrous (Found: C, 11·7; H, 4·1; N, 13·8; S, 31·5; Cu, 15·6. $C_4H_{16}O_6N_4S_4Cu$ requires C, 11·8; H, 3·95; N, 13·7; S, 31·4; Cu, 15·6%). The well-defined, prismatic crystals of this complex tetrathionate were permanent in air, but on heating at 160° they decomposed with blackening. The aqueous solution was stable even on boiling; silver nitrate gave a white precipitate which darkened rapidly; barium chloride had no effect, sodium hydroxide changed the colour from purple to blue, and mineral acids discharged it.

The foregoing complex salts of the oxy-acids of sulphur were all insoluble in alcohol and other organic media.

Attempts made to complete this series of polythionates by the preparation of an ethylenediamminocupric pentathionate were unsuccessful, owing to the destructive action of the diamine in removing sulphur from the alkali pentathionates obtained from Wackenroder's solution.

Bisethylenediamminocupric Selenocyanate, $[Cu,2\ en](CNSe)_2$.—To an aqueous solution of 5·19 g. of cupric chloride and 3·6 g. of ethylenediamine were added 8·6 g. of potassium selenocyanate, also dissolved in water. The purple solution was concentrated to a small bulk and cooled; bluish-purple, prismatic crystals of the complex

selenocyanate then separated. By recrystallisation from water, large, compact crystals were obtained, which were dried over sulphuric acid (Found: C, 18·3; H, 4·2; N, 21·8; Se, 39·8; Cu, 16·6. $C_6H_{16}N_6Se_2Cu$ requires C, 18·3; H, 4·1; N, 21·3; Se, 40·2; Cu, 16·1%).

This complex cupric selenocyanate was stable in air at the ordinary temperature, but it darkened at 100° and melted at 159—160° to a deep blue liquid. The salt was moderately easily soluble in water to a purple solution, which could be boiled without change; it was only slightly soluble in alcohol. With either aqueous or alcoholic solutions, silver nitrate gave a copious white precipitate even in the cold. Mineral acids caused the deposition of elemental selenium. Aqueous or alcoholic soda did not effect any change in the cold, but on warming the alcoholic solution a precipitation of cupric oxide occurred.

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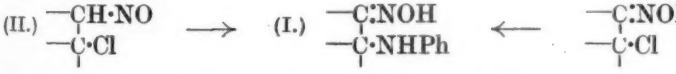
CLXXVI.—*The Recovery of Pinene from its Nitrosochloride.*

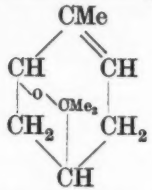
By JOHN CAMPBELL EARL and JAMES KENNER.

THE observation by Wallach (*Annalen*, 1889, **252**, 132; 1890, **258**, 343), that pinene can be regenerated from its nitrosochloride by heating this with aniline, has remained unique until the present time. All other nitrosochlorides which have been examined in this respect furnish nitrolanilides (I) :—

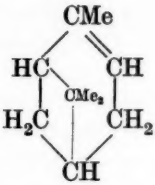


This applies equally to the bisnitrosochlorides such as those of limonene and pinol, which dissociate to a greater or less extent in solution into the unimolecular, blue nitroso-compounds (II), and also to the *iso*nitrosochlorides (III) exemplified by pinol *iso*nitrosochloride (Wallach and Sieverts, *Annalen*, 1899, **306**, 278). The nitrosochloride of trimethylethylene also exists in the two forms (Schmidt, *Ber.*, 1902, **35**, 3727), and again from each of these we have obtained by reactions conducted at the ordinary temperature a nitrolanilide agreeing in properties with that prepared by Schmidt from the nitrosonitrate (*Ber.*, 1902, **35**, 2339; also Wallach, *Annalen*, 1887, **241**, 296). These results, together with the close structural relationship of both pinol (IV) and trimethylethylene (V) to pinene

(VI), only serve to accentuate the exceptional nature of the reaction between aniline and pinene nitrosochloride.

(IV.) 

(V.)

 (VI.)

There is one class of nitrosochlorides the behaviour of which with aniline has not been investigated previously, namely, those which are constitutionally unable to pass into the *iso*nitroso-form. The derivatives of tetramethylethylene (VII) and γ-terpinyl acetate (VIII) were therefore examined in this respect, and both reproduced the behaviour of pinene.

(VII.)

$$CMe_2{:}C\begin{<}CH_2{\cdot}CH_2\\CH_2{\cdot}CH_2\end{>}C\begin{<}Me\\OAc\end{>} \quad \text{(VIII.)}$$

The parent unsaturated compounds were recovered and identified by reconversion into the characteristic nitrosochlorides, and diazoaminobenzene was the other product of the reaction. But the velocity of reaction is much less in these cases than in that of pinene nitrosochloride, a difference which must be ascribed in part to the readiness with which the latter compound loses hydrogen chloride. For, as we have found, it is converted into nitrosopinene by simply boiling its solution in carbon tetrachloride, whereas Schmidt and Leipprand (*Ber.*, 1904, **37**, 545) observed that the nitrosobromide of tetramethylethylene is only slowly acted upon by aqueous potassium hydroxide. It is known that acids assist the condensation of aniline with nitrosobenzene, and, correspondingly, a comparative experiment showed that the interaction of aniline and tetramethylethylene nitrosochloride is accelerated by the addition of aniline hydrochloride at the outset. Even then, however, the velocity of reaction is much less than in the case of the pinene derivative, a point which will be referred to in more detail later.

Not only does hydrogen chloride accelerate, but it actually determines the course of the reaction in the case of pinene nitrosochloride. The formation of "nitrolamines" by the action of piperidine and the aliphatic amines (Wallach, *Annalen*, 1887, **241**, 296; 1888, **245**, 253; 1889, **252**, 107; 1891, **262**, 327) may be attributed to the greater efficiency of these bases, compared with aniline, in neutralising the hydrogen chloride which is necessarily liberated. For, as has now been found, *pinene nitrolanilide* is obtainable by allowing the interaction of the nitrosochloride and aniline to take place in the presence of either pyridine or sodium

acetate. It is, however, essential that these reagents should be employed in a homogeneous solution. For when the reaction was allowed to proceed in chloroform solution in presence of either anhydrous sodium acetate or crystalline lead acetate, diazoaminobenzene was formed. This observation was, however, of value in that diazoaminobenzene had apparently not previously been isolated as such from this reaction, but only after conversion into aminoazobenzene.*

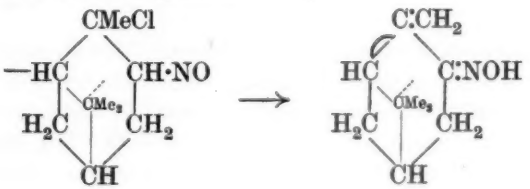
It would therefore seem that, whereas in nitrolanilide formation the chlorine is the first point of attack by the base, Wallach's reaction is due to the preferential reactivity of the nitroso-group, aided by a small proportion of hydrogen chloride derived from the chlorine atom :

$$C_7H_{12}\begin{cases}\text{CMeCl}\\\text{CH·NO}\end{cases} \longrightarrow C_7H_{12}\begin{cases}\text{CMeCl}\\\text{CH·N:NPh}\end{cases} \longrightarrow C_7H_{12}\begin{cases}\text{CMe·NHPh}\\\text{CH·N:NPh}\end{cases}$$

(IX.) (X.)

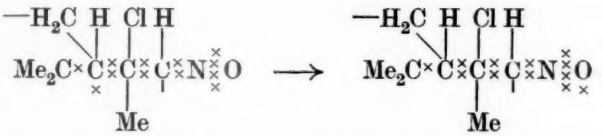
The question whether the diazoaminobenzene originates in the reaction by the coupling of aniline with benzenediazonium chloride eliminated from the preliminary condensation product (IX), or from an anilide (X) derived from the latter, is for the present left in abeyance.

It remains to be explained why pinene nitrosochloride, in its usual behaviour towards aniline, ranges itself with the nitrosochlorides of tetramethylethylene and γ-terpinyl acetate rather than with those compounds to which its formula shows it to be more closely related, and which are capable of transition into the *iso*nitroso-form. It seems obvious that the reason for this peculiarity must be sought in the strained condition of the bonds uniting the central atom of the *gem*-dimethyl group with the rest of the pinene molecule. This produces a state of unsaturation which asserts itself in the conversion of pinene into sobrerol, and is very possibly responsible for the readiness, already mentioned, with which pinene nitrosochloride is converted into nitrosopinene :

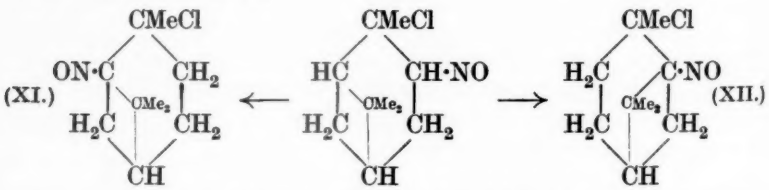


* In quite another direction also, this matter is one requiring further attention, since, in each of the experiments made, the diazoaminobenzene was first isolated in the labile form described by Walther (*J. pr. Chem.*, 1897, **55**, 551).

If, now, this unsaturation be transmitted as a general polar effect along the chain to the nitroso-group, the conditions are such as to enhance the unsaturation of the nitroso-group, as indicated by the following scheme (compare Robinson, *J. Soc. Chem. Ind.*, 1925, 456T) :



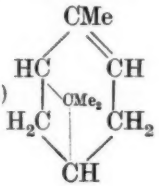
It is therefore conceivable that the nitroso-group may be so reactive as to condense with aniline before passing into the *iso*nitroso-condition. At the same time, it must be emphasised that in the cases of pinol nitrosochloride and trimethylethylene nitrosochloride, already mentioned, where both forms are known, the nitroso- as well as the *iso*nitroso-isomerides are converted by aniline into nitrolanilides. Further, it is agreed that transmission of electronic displacement does not occur so readily through a saturated as through an unsaturated chain. For these reasons, it seems more plausible to assume that the condensation with aniline is preceded by a molecular rearrangement of the nitrosochloride such as to render it formally analogous to those compounds which it resembles in behaviour, and to confer the condition of unsaturation, already mentioned, on the carbon atom directly attached to the nitroso-group. These results would be achieved by the change of the nitrosochloride into (XI), involving migration of the nitroso-group and a hydrogen atom, or into (XII) by interchange of hydrogen and the *gem*-dimethyl group :

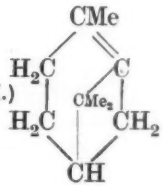


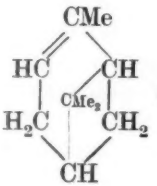
An $\alpha\gamma$-change of this type is most probably involved in the formation of β- from α-dichlorocamphane under the influence of phosphorus pentachloride below 0°, and of *iso*fenchyl from fenchyl alcohol (Meerwein and Wortmann, *Annalen*, 1923, **435**, 190), and perhaps also in the generation of inactive pinol from active sobrerol by hot dilute mineral acids.

Of the alternatives (XI) and (XII), the latter is perhaps preferable, since lability of the *gem*-dimethyl group may, for the reasons already indicated, be expected to be greater than that of the nitroso-group.

The product (XIII), derived from (XII) by elimination of the elements of nitrosyl chloride, must, according to Bredt's rule (*Ber.*, 1902, **35**, 1286), suffer a rearrangement, and this might lead either to α- or to β-pinene. But the easy conversion of β- into α-pinene by various means (Austerweil, *Bull. Soc. chim.*, 1926, **39**, 695; Delépine, *ibid.*, pp. 1475, 1479; Richter and Wolff, *Ber.*, 1926, **59**, 1733) makes it clear that the disturbed system arising from (XI) should settle down into an α-pinene. Lynn (*J. Amer. Chem. Soc.*, 1919, **41**, 361) has shown experimentally that the optically active nitrosochloride obtainable at low temperatures from active pinene reverts, on treatment with aniline, to a hydrocarbon having the same rotatory power as that originally used. The substance (XIII) can conform to this result only if interchange of the *gem*-dimethyl group and a hydrogen atom occurs. The simpler migration of a hydrogen atom would lead to the enantiomorph (XV) of the original pinene (XIV).

(XIV.) 

(XIII.) 

 (XV.)

EXPERIMENTAL.

Action of Aniline on Trimethylethylene Nitrosochloride, m. p. 74—75°.—A solution of the nitrosochloride (3 g.) in chloroform (50 c.c.) was allowed to remain with aniline (7 g.) at the ordinary temperature for 17 hours. The resulting crystalline mass was dissolved by addition of water and more chloroform, and the anilide isolated from the chloroform solution by evaporation of the solvent at the ordinary temperature. After purification in the usual manner by solution in acetic acid and precipitation by ammonia, the crystalline product (3·7 g.) melted at 143° (Found, by micro-analysis: N, 14·3. $C_{11}H_{16}ON_2$ requires N, 14·5%).

Action of Aniline on Trimethylethylene iso*Nitrosochloride*, m. p. 48—49°.—The change of the nitrosochloride, m. p. 74—75°, to its *iso*nitroso-isomeride requires the closest adherence to the conditions prescribed by Schmidt (*Ber.*, 1902, **35**, 3734). For example, in one experiment in which stirring of the hot mass was momentarily neglected, a syrupy product insoluble in light petroleum was obtained in place of the crystalline *iso*nitroso-compound. Similar material is also gradually produced when the nitrosochloride is kept even at 0° in a stoppered bottle.

The *iso*nitrosochloride, m. p. 46—47° (0·45 g.), chloroform (5 c.c.), and aniline (0·62 g.) were allowed to react, and the product isolated, precisely in the manner just described for the nitroso-chloride. The crystalline product (0·48 g.) melted at 143° and did not depress the melting point of the above material.

Action of Aniline on the Nitrosochloride of Tetramethylethylene.—In place of the method described by Thiele (*Ber.*, 1894, **27**, 455) tetramethylethylene was prepared much more conveniently and economically by the conversion of amylene hydrate successively into trimethylethylene, its chlorohydrin, and dimethyl*iso*propylcarbinol, which was then dehydrated. Details of the procedure will be published elsewhere by one of us (J. C. E.).

(*a*) When a mixture of the nitrosochloride (2 g.), excess of aniline (6 c.c.), and alcohol (16 c.c.) was boiled under reflux, the green colour disappeared completely in 5 minutes. After a further 5 minutes, one half of the solution was cooled, treated with concentrated hydrochloric acid (6 c.c.), and kept at 0° for 2 hours. Aminoazobenzene hydrochloride (0·4 g.) was then collected and identified by liberation of the base, m. p. 119°. After crystallisation from alcohol, this, alone or mixed with authentic aminoazobenzene, melted at 124°.

An attempt to isolate the hydrocarbon from the other portion of the solution by distillation in steam was unsuccessful. Modified conditions of experiment were therefore devised for this purpose.

(*b*) A solution of the nitrosochloride (3 g.) and aniline (7 g.) in xylene (30 c.c.) was heated under reflux in boiling water for 40 minutes. By fractionation with a bead column a volatile fraction was obtained, from which, on redistillation, the hydrocarbon (1·3 c.c., b. p. 73—83°) was isolated. It was identified by conversion into the characteristic blue nitrosochloride (1·0 g.), m. p. 119—120°, which did not depress the melting point of the original material.

(*c*) A solution of the nitrosochloride (1 g.) and aniline (1·24 g.) in alcohol (15 c.c.) was divided into two equal portions. After the addition of aniline hydrochloride (0·5 g.) to one portion, both were left at the ordinary temperature for 3½ hours. Each portion then still retained a green colour, but that to which the hydrochloride had been added was perceptibly tinged with yellow. The difference in colour of the two became very much more marked when they were immersed side by side in a bath at 56—60°; after 10 minutes, the one containing the hydrochloride was orange brown, whilst the other still retained a green shade.

Action of Aniline on the Nitrosochloride of γ-Terpinyl Acetate.—The melting point of this nitrosochloride was given by Baeyer (*Ber.*, 1894, **27**, 445) as 82°, but material which had been repeatedly

purified by precipitation from alcoholic solution by addition of water as recommended by Baeyer usually melted at about 77°. The discrepancy is perhaps attributable to polymerisation, since a sample which had been preserved for several weeks and again recrystallised was almost colourless and melted at 95° (Found, by micro-analysis : N, 5·2. Calc. for $C_{12}H_{20}O_3NCl$: N, 5·3%).

A mixture of the nitrosochloride (1 g.), aniline (0·36 g.), and alcohol (25 c.c.) became deep red when boiled under reflux for 35 minutes. By distillation in steam, a yellowish oil (0·5 c.c.) was isolated from which a blue nitrosochloride (0·12 g.) was obtained. This melted at 76° after precipitation from alcoholic solution by means of water, and did not depress the melting point of the original nitrosochloride.

Formation of Nitrosopinene from Pinene Nitrosochloride.—When a solution of the nitrosochloride (2 g.) in carbon tetrachloride (40 c.c.) was heated, depolymerisation was indicated by the development of a blue colour. This, however, disappeared almost immediately, presumably owing to formation of the *iso*nitroso-isomeride, and at the same time evolution of hydrogen chloride set in. After boiling for 2 minutes, the solution was cooled, and the solvent was allowed to evaporate at the ordinary temperature. By maceration of the sticky residue with ice-water, hydrochloric acid was removed. After further purification by crystallisation from light petroleum, nitrosopinene (0·38 g.), m. p. 131°, was obtained.

Pinene Nitrolanilide.—(*a*) A mixture of pinene nitrosochloride with a solution of crystallised sodium acetate (10 g.) and aniline (2·3 g.) in alcohol (150 c.c.) was boiled for 5 minutes and cooled, and excess of ice-water added. A sticky mass separated and gradually solidified. After reprecipitation by addition of ammonia to a diluted and filtered solution of the material in glacial acetic acid, it was further purified by crystallisation from light petroleum. The *anilide* was thus obtained in small, yellowish, hexagonal prisms (1·95 g.), m. p. 122° (Found, by micro-analysis : N, 10·6. $C_{16}H_{22}ON_2$ requires N, 10·8%).

(*b*) A solution of the nitrosochloride (1 g.) in chloroform (15 c.c.) was added to a mixture of aniline (0·46 g.) and pyridine (2 g.) in chloroform (5 c.c.) at 20°. After 16 hours, the solution was washed with water, dried over sodium sulphate, and allowed to evaporate at the ordinary temperature. After purification in the manner just described, the anilide (0·2 g.) was obtained crystalline, m. p. 121°, and did not depress the melting point of material prepared by the preceding method.

Diazoaminobenzene from Pinene Nitrosochloride.—As an alternative to the procedures just described, a solution of the nitrosochloride (2 g.) in chloroform (30 c.c.) was shaken with aniline

(0·92 g.) in presence of finely powdered, crystalline lead acetate (3·8 g.) at the ordinary temperature for 2½ hours. After filtering from lead chloride, the solution was allowed to evaporate at the ordinary temperature. Unchanged nitrosochloride (0·92 g.), m. p. 109—110°, remained after extraction of the residue with alcohol. The cooled alcoholic solution deposited yellow needles (0·5 g.), m. p. 79—80°, on careful dilution with water.

This material represented the labile form of diazoaminobenzene, to which Walther ascribed the melting point 79—81° (*J. pr. Chem.*, 1897, **55**, 551). The material melted at 91—92° (Found : N, 21·2. Calc. : N, 21·3%) after crystallisation from alcohol, and at 98° after further crystallisation from ligroin.

Exactly similar phenomena resulted from the use of anhydrous sodium acetate in place of lead acetate.

THE UNIVERSITY, SYDNEY. [*Received, March 16th*, 1927.]

CLXXVII.—*Researches in the Menthone Series. Part IV.* iso*Menthols and* iso*Menthones.*

By JOHN READ, GEORGE JAMES ROBERTSON, and ALISON MARY RITCHIE COOK.

OF the four possible externally compensated menthols, the two derived from *dl*-menthone—namely, *dl*-menthol (m. p. 34°) and *dl-neo*menthol (m. p. 51°)—were characterised in 1912 by Pickard and Littlebury (J., **101**, 109). Much uncertainty has existed, however, respecting the two remaining compounds, *dl-iso*menthol and *dl-neoiso*menthol, derived from *dl-iso*menthone. Bedos (*Bull. Soc. chim.*, 1926, **39**, 674) claims to have demonstrated the existence of the four racemic menthols and the two corresponding racemic menthones through a study of the interaction between magnesium *iso*propyl bromide and the two isomeric 2-chloro-5-methyl*cyclo*hexanols. This claim is open to serious criticism. In the first place, neither of the supposed new menthols was crystalline, whereas we show below that *dl-iso*menthol, prepared by the action of nitrous acid upon *dl-iso*menthylamine (J., 1926, 2232), melts at 53·5°. Secondly, the menthol prepared by Bedos from either of the above sources, or by the action of magnesium *iso*propyl bromide on the oxide of methyl-Δ^3-*cyclo*hexene, gave an inactive menthone which, from its inability to furnish crystalline derivatives, was neither pure *dl*-menthone nor *dl-iso*menthone (compare Read and Cook, J., 1925, **127**, 2783). Thirdly, the base obtained by reducing the liquid oxime of this menthone corresponded in no particular with *dl-iso*menthylamine (J., 1926, 2230).

In the present communication, we show that the mixture of menthols obtained in the reduction of *dl*-piperitone by sodium and alcohol contains *dl*-menthol as well as *dl-iso*menthol; the mixture is being further examined with the object of isolating the other two stereoisomerides. By the action of nitrous acid on *d*- and *l-iso*menthylamine, derived through *d*- and *l-iso*menthone from *l*- and *d*-piperitone, we have also been able to prepare *d*- and *l-iso*menthol. The constants for the *d*-component, m. p. 81·5°, $[\alpha]_D^{15}$ + 27·0° in alcohol, are in satisfactory agreement with the data recorded by Beckmann (*Ber.*, 1909, **42**, 846) for *d-iso*menthol derived ultimately from the oxime of " inverted " *l*-menthone, the values being m. p. 83°, $[\alpha]_D$ + 26·3°. Moreover, Zeitschel and Schmidt (*Ber.*, 1926, **59**, 2298) have recently recorded m. p. 85°, $[\alpha]_D$ + 23·6°, for a specimen of *d-iso*menthol of unspecified origin. The form of the melting-point curve of mixtures of the *d*- and *l*-modifications is that of a conglomerate. *dl-iso*Menthol has a melting point only slightly higher than that of *dl-neo*menthol, but whilst *d*- and *l-neo*menthol are oils the optically active *iso*menthols have a melting point 28° higher than that of the externally compensated form; *d*- and *l*-menthol also melt at a higher temperature than *dl*-menthol. These relationships, which are of particular interest in view of the apparent configurational resemblance between the menthols and the *iso*menthols (compare J., 1926, 2213), point to the possibility of *d*- and *l-neoiso*menthol displaying a lower melting point than *dl-neoiso*menthol.

The *iso*menthols now described provide the only sources at present available for the preparation of practically pure specimens of *dl-iso*menthone and its optically active components. Although *l*- and *d*-piperitone upon catalytic hydrogenation yield preparations of *d*- and *l-iso*menthone with values of $[\alpha]_D^{15}$ as high as ± 70°, it has been pointed out in an earlier communication (J., 1926, 2211) that the optical purity of such preparations is unsatisfactory. Since Beckmann's chromic acid mixture has little inverting action on *d-iso*menthone (*loc. cit.*, p. 2215), it was anticipated that careful oxidation of the *iso*menthols with this reagent would furnish the corresponding *iso*menthones in a state of approximate purity. A specimen of *d-iso*menthone prepared in this way had $[\alpha]_D^{15}$ + 91·7°, a value which agrees satisfactorily with $[\alpha]_D$ + 93·2°, observed by Beckmann (*loc. cit.*; compare also Barrowcliff, J., 1907, **91**, 875, and Zeitschel and Schmidt, *loc. cit.*). This ketone gives a viscid oxime, whilst the melting points recorded for the semicarbazone range from 154° (Beckmann) to 164° (Zeitschel and Schmidt). The semicarbazone prepared by us, when recrystallised once from light petroleum containing a little methyl alcohol, formed minute needles

melting indefinitely at 125—138° and having $[\alpha]_D^{15°}$ + 23·8° in absolute alcohol (c = 1·5); the isolation of a homogeneous derivative from this product proved so tedious that we recommend the characterisation of *d-iso*menthone by means of the hydrochloride of the oxime, which is readily obtained in well-defined prisms, m. p. 132°, $[\alpha]_D^{15°}$ + 38·6° in chloroform (c = 4·0).

It is probable that preparations of *d*- (or *l*-)*iso*menthone made as indicated still contain a small proportion of *l*- (or *d*-)menthone, but accepting the values $[\alpha]_D^{15°}$ + 91·7° and $[\alpha]_D^{20°}$ − 29·6° for *d-iso*menthone and *l*-menthone, respectively, it now becomes possible to calculate with a close approximation to accuracy the composition of various equilibrium mixtures of these two readily interconvertible ketones (J., 1926, 2210). Thus, when equilibrated with alcoholic sodium ethoxide, *l*-menthone gave a mixture containing only 30% of *d-iso*menthone; this proportion rose to 37% when the ketone was maintained at 200°, and to 46% when it was treated with melting 90% sulphuric acid. Furthermore, *d*-pulegone and *l*-Δ^4-*p*-menthen-3-one, when hydrogenated in presence of colloidal palladium (*loc. cit.*), yielded mixtures containing, respectively, 52% and 60% of *d-iso*menthone; whilst the product furnished by *l*- (or *d*-)piperitone contained as much as 82% of *d*- (or *l*-)*iso*menthone, the absence of *dl*-piperitone from the preparations used being assumed.

Although the isolation of pure derivatives of *dl-iso*menthone has been described in these researches (J., 1926, 2783), it has hitherto been impossible to obtain the pure ketone, owing to the inversion which accompanies its regeneration from such derivatives. *dl-iso*Menthone may now be made, however, through the oxidation of *dl-iso*menthol; the preparation of the ketone by this method, for the purpose of determining its physical constants, is at present engaging our attention.

Owing to their method of formation, we regard the *iso*menthols as corresponding in molecular configuration to the *iso*menthylamines. In the configurational scheme recently advanced for the menthylamines (J., 1926, 2213), the *cis*- and *trans*-configurations were adopted for menthones and *iso*menthones, respectively. Measurements of the parachors (compare Sugden and Whittaker, J., 1925, **127**, 1868) recently made by Dr. P. G. Carter in this College indicate, however, that the menthones and *iso*menthones possess the *trans*- and *cis*-configurations, respectively, the mean values of [*P*] being determined as follows: *dl*-menthone, 400·9; *l*-menthone, 403·2; *dl-iso*menthone, 405·3; *d-iso*menthone, 404·6. The calculated value for $C_{10}H_{18}O$, 1 non-polar double bond, 1 six-membered ring, is [*P*] 405·1. The specimens of *iso*menthone used

for these measurements were prepared by the catalytic hydrogenation of *dl*- and *l*-piperitone, and were thus contaminated with the corresponding menthones, as indicated above. The results agree broadly with the observations of Zeitschel and Schmidt (*loc. cit.*), who found that *d-iso*menthone gave slightly higher values for refractive index and density than *l*-menthone; the Auwers–Skita rule thus favours the *trans*-configuration for menthone, although the question cannot yet be considered as decisively settled.

Experimental.

dl-iso*Menthol and its Optically Active Components.*—dl-iso*Menthol.* *dl-iso*Menthylamine hydrochloride (26·6 g.), obtained by reducing *dl-iso*menthoneoxime (J., 1926, 2230), when recrystallised twice from hot acetone containing a little methyl alcohol and then treated with sodium nitrite (10 g.) in aqueous solution at 70°, yielded a partly crystalline product (14·0 g.), which was forthwith distilled in steam. A fraction (8·7 g.) of the dry material distilling at 95—100°/10 mm. and having $n_D^{16°}$ 1·4660 deposited crystalline dl-iso*menthol* (2·6 g.) at the ordinary temperature; after being kept for a few days on porous plate in a desiccator, this substance was obtained in small, glistening needles, m. p. 53·5°, with an odour similar to but considerably milder than that of *l*-menthol. The hydrochloride (33 g.) of the base formed on reducing the viscid mother-liquor from crystalline *dl*-menthoneoxime (*loc. cit.*, p. 2231) yielded a liquid mixture of menthols when treated similarly with nitrous acid; the bulk (14·5 g.) of the product distilled at 95—110°/20 mm. and had $n_D^{16°}$ 1·4660, but it proved impracticable to isolate crystalline material either from this fraction or from a refractionated portion (1·8 g.) having b. p. 97—100°/10 mm. and $n_D^{16°}$ 1·4665. dl-iso*Menthyl hydrogen phthalate*, prepared by the method of Pickard and Littlebury (J., 1912, **101**, 113), crystallised from light petroleum containing a little ether in small clusters of minute prisms, m. p. 107—108° (Found: *M*, by titration, 301. $C_{18}H_{24}O_4$ requires *M*, 304). *dl-iso*Menthol regenerated from this derivative by hydrolysis with hot alcoholic sodium hydroxide melted unchanged at 53·5°. The *hydrogen succinate* was obtained in the form of an oil which yielded a crystalline mass on cooling and seeding with the supposed *dl-iso*menthyl hydrogen succinate (m. p. 72—73°) described below; as the material was very soluble in organic solvents and available only in small amount, a satisfactory purification of this specimen could not be effected (*vide infra*). The *phenylurethane* was liquid at the ordinary temperature.

d-iso*Menthol.* Crude *d-iso*menthylamine hydrochloride (120 g.), prepared from the viscid oxime of *d-iso*menthone (J., 1926, 2221)

and having $[\alpha]_D^{15°}$ + 20·6° in aqueous solution, was dissolved in a hot mixture of acetone (1200 c.c.) and methyl alcohol (175 c.c.). The first two fractions to separate (40·4 g.) consisted of pure *d-iso*menthylamine hydrochloride, having $[\alpha]_D^{15°}$ + 23·6° in aqueous solution (c = 2·3), whilst the residue, upon fractional crystallisation from acetone, followed by ethyl acetate, yielded a further quantity (11·8 g.) of this substance. The more soluble fractions of the material gave values of $[\alpha]_D$ ranging from + 17·2° to + 18·9° in aqueous solution.

Upon treating *d-iso*menthylamine hydrochloride (20 g.) in cold aqueous solution with the calculated amount of sodium nitrite, a crystalline separation of the nitrite of the base was obtained. The mixture was warmed to 70° and finally heated on the water-bath until the evolution of nitrogen ceased. When distilled with steam, the oily product (11·4 g.) crystallised partly in the receiver. About 15% of the original *d-iso*menthylamine was recovered unchanged. After two successive fractional distillations of material (28·8 g.) obtained in this way, the first fraction (4·9 g.) had b. p. 54—58°/12 mm., $n_D^{15°}$ 1·4583, and $\alpha_D^{15°}$ + 27·2° (l = 1); whilst the fourth fraction (12·4 g.), which became almost wholly crystalline, had b. p. 96—98·5°/11 mm. These fractions consisted, respectively, of approximately pure *d*-Δ^3-menthene (partly racemised) and *d-iso*menthol, and the intermediate fractions were composed of mixtures of these two substances. After purification on porous plate, d-iso*menthol* was obtained in small needles, m. p. 81·5°, $[\alpha]_D^{15°}$ + 24·0° in benzene (c = 2·5), $[\alpha]_D^{15°}$ + 27·0° in absolute alcohol (c = 1·8). The odour was indistinguishable from that of *dl-iso*menthol. d-iso*Menthyl hydrogen phthalate* crystallises from methyl alcohol in aggregates of small prisms, m. p. 107·5—108·5°, $[\alpha]_D^{15°}$ + 27·5° in chloroform (c = 3·4). The *hydrogen succinate* was obtained as a yellowish, viscid liquid, $[\alpha]_D^{15°}$ + 22·5° in chloroform (c= 3·8).

The above and other experiments indicated that *d-iso*menthylamine reacts with nitrous acid to form *d*-Δ^3-menthene and *d-iso*menthol in the approximate ratio of 1 to 2, the combined yield being about 80% of the calculated amount. Only about one-third of the *d-iso*menthol formed was actually isolated in the pure crystalline condition.

l-iso*Menthol*. *l-iso*Menthylamine hydrochloride (6 g.), prepared in the way already described (J., 1926, 2222), and having $[\alpha]_D^{15°}$ — 22·6° in dilute aqueous solution, was treated with nitrous acid as described above. The fraction (0·8 g.) of the product boiling at 103—107°/19 mm. rapidly became crystalline, and when purified on porous plate yielded l-iso*menthol*, m. p. 80·5°, $[\alpha]_D^{15°}$ — 24·1° in absolute alcohol (c = 1·8).

Melting-point Curve of Mixtures of d- *and* l-iso*Menthol.*—Mixtures of *d-iso*menthol (m. p. 81°) and *l-iso*menthol (m. p. 79·5—80·5°) of known compositions were prepared by direct weighing. In each case the mixture was gently fused, with stirring, the melting point being then observed in the usual way for the resolidified material. Several observations were made in each instance, and the melting points were found to be well defined and consistent. Mixtures containing 100, 89·6, 73·6, 60·1, 50·0, and 26·3% of *d-iso*menthol melted at 81·5°, 77°, 67—68°, 58—59°, 51·5°, and 65°, respectively. The corresponding melting-point curve appears to conform, within the limits of experimental error, to Roozeboom's Fig. 6 (*Z. physikal. Chem.*, 1899, **28**, 507). The observed melting point for the equimolecular mixture of *d-* and *l-iso*menthol (51·5°), which must thus be regarded as a conglomerate, agrees satisfactorily with the value recorded above for *dl-iso*menthol prepared directly from *dl-iso*menthylamine. No depression was observed in the melting point of a mixture of specimens of *dl-iso*menthol prepared in these two ways.

Preparation and Characterisation of Optically Pure d-iso*Menthone.*—*d-iso*Menthol (4 g.), m. p. 81·5°, $[\alpha]_D^{15°}$ + 24·0° in benzene, was added to Beckmann's chromic acid mixture at 30° (compare *Annalen*, 1889, **250**, 325). Upon shaking the mixture vigorously, the temperature rose to 50°, at which point the black chromium derivative decomposed. The resulting *d-iso*menthone was at once extracted from the cooled mixture with ether, the extract being then washed four times with water and dried over sodium sulphate. The treatment with dilute sodium hydroxide solution, adopted by Beckmann, was omitted. The crude product (3·3 g.) had $n_D^{16°}$ 1·4555, and represented 82·5% of the calculated yield. The first fraction (2·75 g.), distilling at 86—87°/12 mm., was regarded as pure d-iso*menthone*. It had $n_D^{16°}$ 1·4545, $\alpha_D^{15°}$ + 82·16°, $[\alpha]_D^{15°}$ + 91·7° (assuming $d = 0·896$; compare J., 1923, **123**, 2922). The odour was less penetrating than that of *l*-menthone.

Part of the ketone so prepared was oximated in aqueous-alcoholic solution with hydroxylamine acetate, sodium bicarbonate having been added beforehand until the solution was only faintly acid to litmus. After 3 days, d-iso*menthoneoxime* was precipitated by the addition of water and extracted with ether. When freed from the last traces of the solvent, it was obtained as a colourless, viscid oil, having $n_D^{17°}$ 1·4830 and $[\alpha]_D^{15°}$ + 45·1° in absolute alcohol ($c = 2·2$). The oil could not be induced to crystallise by applying any of the usual methods. When cooled in liquid air, either alone or in contact with light petroleum, it gave a brittle, vitreous mass, which reverted to a viscid liquid at the ordinary temperature. The

p-*nitrobenzoyl* derivative is an oil. d-iso*Menthoneoxime hydrochloride*, obtained by passing dry hydrogen chloride into a cooled ethereal solution of the oxime, is the most characteristic derivative of *d-iso*menthone yet prepared. It crystallises from acetone containing a little absolute alcohol in large, transparent prisms of tabular habit, m. p. 132°, $[\alpha]_D^{15°}$ + 38·6° in chloroform ($c = 4·0$). With care, crystals of this substance might be characterised goniometrically. The hydrochloride reverts completely to its components in presence of water. A further purification of the oxime was therefore attempted by shaking an ethereal solution of this derivative with water containing an equivalent amount of sodium bicarbonate. After drying in a vacuum at 60°, the resulting viscid liquid had $n_D^{14°}$ 1·4865, and $[\alpha]_D^{15°}$ + 46·0° in absolute alcohol ($c = 3·8$).

In the course of the above characterisation of *d-iso*menthone, the following related derivatives were prepared for purposes of comparison. dl-iso*Menthoneoxime hydrochloride* crystallises from acetone in clusters of transparent prisms, m. p. 127—128° (decomp.). dl-*Menthoneoxime hydrochloride* cannot be recrystallised in the ordinary way, owing to the ease with which it is hydrolysed in presence of moisture. After being washed with anhydrous ether and dried on porous plate in a vacuum, it was obtained in minute needles, m. p. 94°. l-*Menthoneoxime hydrochloride*, purified similarly, formed long, slender prisms, m. p. 118—119°, $[\alpha]_D^{15°}$ − 89·1° in chloroform ($c = 2·1$). The p-*nitrobenzoyl* derivative of *l*-menthoneoxime was prepared by heating equivalent amounts of the oxime and *p*-nitrobenzoyl chloride in pyridine solution on the water-bath; it separated from alcohol in pale yellow needles, m. p. 102·5°.

Attempts to prepare neoiso*Menthols and* neoiso*Menthylamines.*— 1. The liquid mixture of menthols obtained by the reduction of *dl*-piperitone with sodium and absolute alcohol (J., 1925, **127**, 2784), when freed from *dl*-α-phellandrene, distilled at 90—97°/8·5 mm. and had $n_D^{15°}$ 1·4675. Treatment with phthalic anhydride (J., 1912, **101**, 113) yielded a partly crystalline mass (140 g.), which was fractionally crystallised from light petroleum, with the addition of a little absolute alcohol when necessary. The first two fractions melted at 107—112° (40 g.) and 82—87° (49 g.), respectively, whilst the residue was a viscid liquid. After three recrystallisations, the first fraction yielded large, transparent plates, which showed no alteration of melting point (131—132°) when mixed with *dl*-menthyl hydrogen phthalate. The original mixture thus contained some *dl*-menthol. The second fraction of the phthalate upon similar treatment yielded rosettes of soft needles, m. p. 93—94°, which upon hydrolysis with alcoholic sodium hydroxide yielded a menthol, m. p. 46—47°. A mixture of this preparation with pure *dl-iso-*

menthol (m. p. 53—53·5°) melted at 47—52°. The viscid fraction of the phthalate has not yet been examined further.

A specimen of crystalline menthol (m. p. 32—40°), obtained by cooling a portion of the above crude liquid menthol (b. p. 90—97°/8·5 mm.), gave a vitreous mass when heated with phthalic anhydride. Prolonged partial crystallisation from light petroleum furnished two kinds of crystals, the less soluble of which formed opaque clusters of soft needles, m. p. 103—104° (Found: C, 70·7; H, 8·3. $C_{18}H_{24}O_4$ requires C, 71·1; H, 7·9%). A more soluble series of fractions, obtained in larger amount, consisted of hard clusters of glistening prisms, m. p. 91—94° (Found: C, 70·4; H, 7·8%). Both kinds of crystals gave analytical results agreeing with those required for menthyl hydrogen phthalates, and upon hydrolysis yielded specimens of menthol melting at 46—49° and 39—42°, respectively. The corresponding mixed melting points with pure *dl-iso*menthol were 49—53° and 40—52°. The phthalate melting at 103—104° was therefore practically pure *dl-iso*menthyl hydrogen phthalate.

No definite proof of the occurrence of a third crystalline menthol in the reduction product of *dl*-piperitone is provided by the above observations. It may be added that the crude crystalline mixture of menthols, m. p. 32—40°, readily yielded a crystalline product when heated with succinic anhydride; after two recrystallisations from light petroleum, an apparently homogeneous product was isolated in small, colourless plates, m. p. 72—73°. In view of the general behaviour of the menthol from which it was derived, this substance is regarded as dl-iso*menthyl hydrogen succinate* (Found: C, 66·0; H, 9·3. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%).

2. The mother-liquors from the recrystallisation of crude *d-iso*menthylamine hydrochloride (*vide supra*) were examined in various ways. A fraction of the hydrochloride having $[\alpha]_D$ + 18·5° (water) yielded a mixture of menthene and menthol when treated with nitrous acid. A liquid menthol fraction distilling at 93—98°/12 mm. had $n_D^{15°}$ 1·4654 and $[\alpha]_D^{15°}$ + 12·1° in benzene ($c = 3·0$). The corresponding partly crystalline menthol fraction furnished by pure *d-iso*menthylamine hydrochloride had $[\alpha]_D^{15°}$ + 18·5°. The acetyl derivative prepared from the same fraction of the hydrochloride was a viscid liquid having $[\alpha]_D^{15°}$ + 16·2° in chloroform. The crude salicylidene derivative had $[\alpha]_D^{15°}$ + 32·1° in chloroform ($c = 5·5$), m. p. 65—85°. After five recrystallisations from alcohol, the first fraction softened at 85° and melted at 107—112°, whilst the value of $[\alpha]_D^{15°}$ was + 61·1°. From these observations, it appears that the mother-liquors contained *d-iso*menthylamine, together with a lævorotatory base, and possibly also some *dl-iso*menthylamine.

3. The residual uncrystallisable syrup from the preparation of formyl-*d*-*neo*menthylamine (J., 1926, 2218) was hydrolysed with hydrochloric acid. The resulting solid mixture of hydrochlorides (69 g.) was extracted with ether in a Soxhlet apparatus in order to remove *d*-*neo*menthylamine hydrochloride. The residue (48 g.), when recrystallised from acetone containing a little methyl alcohol, gave a first fraction (10·6 g.) having $[\alpha]_D^{15°}$ — 10·7° (water), whilst a final (fourth) fraction (15·2 g.) had $[\alpha]_D^{15°}$ — 5·1°. The rotatory power of the first fraction corresponds to a mixture of 55·4% of *l*-menthylamine hydrochloride and 44·6% of *d*-*neo*menthylamine hydrochloride, it being assumed that no other base was present. This fraction, however, yielded a crude salicylidene derivative, m. p. 48°, having $[\alpha]_D^{15°}$ — 72° (chloroform). The mixture indicated above would yield a product having $[\alpha]_D^{15°}$ — 52·7°, and this would become — 34·6° if the assumed *d*-*neo*menthylamine were replaced by *d*-*iso*menthylamine. It thus appeared that a new lævorotatory salicylidene derivative must be present in the product derived from the first fraction of the hydrochloride. Similar results were obtained with the succeeding fractions, and eventually, after recrystallising the crude salicylidene derivative three times from light petroleum, a homogeneous product was obtained, having m. p. 99—100°, $[\alpha]_D^{15°}$ — 17·9° (chloroform). This substance appears to be the salicylidene derivative of an active form of the hitherto unknown *neoiso*menthylamine (compare J., 1926, 2213, 2225), which base we hope to isolate and characterise in continuing our researches on menthylamines.

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UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD,
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CLXXVIII.—*A Method for the Estimation of Small Quantities of Water in Alcohol.*

By ERNEST LESTER SMITH.

THE methods at present available for the determination of water in alcohol may be divided into two groups: (1) physical methods, comprising the density method and methods depending on the effect

of water on the miscibility of certain liquids with alcohol, such as Crismer's kerosene method (*Bull. Soc. chim. Belg.*, 1904, **18**, 18; also Curtis, *J. Physical Chem.*, 1898, **2**, 371; Nussbaum, *J. Pharm. Chim.*, 1917, **15**, 230; Jones and Lapworth, J., 1914, **105**, 1804); (2) chemical methods depending on the interaction of the water with substances such as calcium hydride (Worth, *Z. Deut. Oel-Fett Ind.*, 1921, **41**, 147), or calcium carbide (Newman, *J. Soc. Chem. Ind.*, 1924, **43**, 285; also Weaver, *J. Amer. Chem. Soc.*, 1914, **36**, 2462; Hartley and Raikes, J., 1925, **127**, 526). The accuracy claimed for the majority of these processes is not greater than 0·03 unit in the percentage of water. A further disadvantage inherent in nearly all the methods is the necessity for calibration with standard alcohol–water mixtures, the preparation of which is a matter of extreme difficulty where very small percentages of water are concerned.

In view of these considerations, an attempt was made to devise a new method. When the sodium or potassium compound of a hydroxylic substance such as phenol or alcohol is dissolved in aqueous alcohol, it is partly hydrolysed with formation of sodium or potassium hydroxide, an equilibrium being set up. If an ester is present, it will be hydrolysed irreversibly by the free alkali; the equilibrium is thereby disturbed and the reaction proceeds until either the alkali compound, the ester, or the water disappears completely. Provided that the concentration of the water is less than that of the other reactants, conditions can be so chosen that the reaction approaches completion with respect to this component in a relatively short time. It is possible by means of an extrapolation method to find the "limiting titration," *i.e.*, the titre at infinite time, and the difference between this and the initial titration is equivalent to the water concentration. Sodium or potassium ethoxide is employed, prepared by dissolving the metal in the alcohol to be tested, and ethyl acetate as the ester.

Experimental.

In carrying out the estimation, it is essential to use perfectly dry apparatus, and to reduce the manipulation of the solutions to the minimum, so as to avoid exposure to the air for more than a few seconds. Hard glass tubes of about 13 c.c. capacity are used as reaction vessels, and are closed with corks soaked in paraffin wax just before use and tied down with string. Finally, the tubes are inverted and dipped into molten paraffin wax for a few seconds, which effectually protects the contents against the possible entrance of water.

Sodium or potassium may be used; if the former, sodium acetate

crystallises in the tubes. This solid does not appear to affect the results, however, the same value being obtained whichever metal is employed.

The solution is prepared as follows : A quantity of the alcohol to be tested (40 to 80 c.c.) is poured into a small, dry, narrow-necked flask. A clean piece of sodium or potassium, large enough to make the solution about $N/2$, is cut under the surface of the oil in which it is kept, and rapidly transferred to the alcohol, without removal of the oil film from the surface of the metal, which is therefore not exposed to the air at all. The trace of oil does not interfere with the estimation. The metal is allowed to dissolve, the flask being closed by a calcium chloride tube and, if necessary, cooled in water. A few c.c. of ethyl acetate (dried over sodium) are now added, and immediately 10 c.c. of the solution are withdrawn by means of a dry pipette, and titrated rapidly. The pipette is fitted with a trap, consisting of a narrow glass tube bent into a loop, and filled with fine granules of calcium chloride, to prevent moisture from the mouth finding its way into the solution. This is next delivered into the tubes with the same pipette, care being taken to replace the cork as soon as a tube is charged. When ready, the tubes are sealed with wax as described, and placed in a bath of water at about 70°. The water is covered with oil to prevent steam arising, and the tubes are supported in a rack so that the corks are not below the surface of the water. In practice, a thermostat was used, but this is not essential. After 10 to 30 minutes, tubes are withdrawn at intervals and cooled in water, and the contents are titrated. It should be found that successive titration values are constant or decrease slightly. In the latter case, the extrapolation method described below must be applied to find the "limiting titration." The difference between the initial and the limiting titration corresponds to the water in the alcohol. If $N/8$-acid is used, this difference, in c.c., multiplied by the factor 0·0225 gives the percentage of water by volume directly.

It is occasionally found that one (or more) of the tubes gives an abnormally low titre, owing to the introduction of a trace of water. Such a reading may be neglected. When the amount of ethyl acetate added exceeds about 1 c.c., the volumes of ester and alcohol are measured approximately and allowance is made for the slight increase in the volume of the solution on addition of the ester. It is assumed that the addition of the alkali metal does not alter the volume.

Two methods have been used for finding the "limiting titration" : (1) the titrations are plotted against time, and the slope of the curve at various points is calculated. The slopes are then plotted against

the corresponding titration values, yielding a nearly straight line which can be extrapolated to zero slope, and the "limiting titration" read off; (2) the titrations are plotted against the reciprocal of the time, giving a similar curve which can be extrapolated to zero 1/Time in the same way. The two methods agree well, the values for percentage of water not differing by more than 0·004%. The second is the simpler and more trustworthy and was used in most cases.

A further modification, which was developed towards the end of the research, allows of still greater simplification. It consists in using a considerable excess of potassium or sodium, and also of ethyl acetate, so that, when the water has nearly disappeared, the concentrations of ethoxide and ester are still large ($N/4$ to $N/2$).

Under these conditions, the reaction is extremely rapid, and proceeds to completion, as nearly as can be estimated, in 10 to 40 minutes at 70°. Thus there is no necessity for extrapolation, and also less material is required, for it is only necessary to take sufficient for two or three tubes, the contents of which are titrated after ½ hour or 1 hour, and should, of course, give the same titration value. Moreover it is not necessary to heat the tubes in a thermostat, since a constant temperature is not necessary. In this form, the method may be described as an indirect titration of water with standard acid. The process is extremely delicate and the accuracy attainable is limited, not by lack of sensitiveness, but by the difficulty of preventing the entry of further traces of moisture into the alcohol during the course of the estimation.

Results.—The following experiments are typical, the first of a case where extrapolation had to be applied, and the second of a case where this was unnecessary.

Sample D.

Sodium used. Water added, 0·335%. Ester volume correction, 3%.

Time (mins.) ...	0	5	10	23	35	58	92	155	∝
Titre ($N/8$-acid)	28·3	14·1	11·4	9·7	9·3	9·05	8·8	8·7	8·6

Diff. = 28·3 − 8·6 = 19·7 c.c.

% Water = 19·7 × 0·0225 × 1·03 = 0·457%.

Sample F.

Potassium used. No water added. Ester volume correction, 5%.

Time	0	10	43	63	113
Titre ($N/4$-acid).....	15·55	13·25	13·2	13·2	13·2

Diff. = 15·55 − 13·2 = 2·35 c.c.

% Water = 2·35 × 0·045 × 1·05 = 0·111%.

The degree of accuracy attainable in this estimation was only to be arrived at by repeating it several times with the same sample

of alcohol. A further check could be obtained by adding a known quantity of water and estimating the total amount present.

The following results have been obtained:

Sample D.

Expt.	% H_2O added.	% H_2O found.	% H_2O originally in alcohol.
1	—	0·117	0·117
2	—	0·122	0·122
3	0·335	0·457	0·122

Sample H.

Expt.	1	2	3
% H_2O in alcohol	0·151	0·162	0·157

Sample I.

Expt.	% H_2O added.	% H_2O found.	% H_2O originally in alcohol.
1	—	0·022	0·022
2	0·158	0·164	0·006
3	0·164	0·176	0·012
4	0·218	0·229	0·011

These results show that it is possible to estimate the water in alcohol by this process to 0·01%. This is, therefore, one of the most accurate processes yet devised for the estimation of small quantities of water in alcohol, and also one of the simplest if the final modification is employed. Moreover, it possesses one outstanding advantage over almost every other method in that the result can be calculated directly from the readings obtained and there is no necessity for calibration against alcohol–water mixtures of known composition.

The author wishes to express his thanks to Dr. Crocker for the great interest he has taken in this research, and to the London County Council for a grant which enabled the work to be undertaken.

CHELSEA POLYTECHNIC. [*Received, April 4th*, 1927.]

CLXXIX.—*A Process for the Dehydration of Alcohol.*

By ERNEST LESTER SMITH.

SINCE the water present in alcohol is very completely consumed in the estimation process described in the preceding paper, it seemed possible that the reaction might be utilised as a method of dehydrating alcohol. Dry ethyl alcohol is a very hygroscopic substance from which it is difficult to remove the last traces of water. The ideal process would be to employ a rapid, irreversible, and preferably homogeneous reaction in which the water is consumed; also the

dehydrating agent and the products of the reaction should be non-volatile so that the alcohol may be distilled off uncontaminated. This ideal is not attained completely by any of the methods in use at present for the preparation of anhydrous alcohol.

The reaction between sodium or potassium ethoxide, an ester, and water in alcohol approaches very close to the ideal suggested, in respect of rapidity, irreversibility and homogeneity. The reactants and products are all non-volatile with the exception of the ester. This difficulty, however, can be surmounted by the use of an ester of high boiling point such as ethyl succinate, from which the alcohol can be separated by fractional distillation. The process evolved is as follows : The alcohol to be dehydrated is contained in a flask, fitted with a fractionating column, attached to a condenser which can be used either for refluxing or for distillation, without disconnexion. The requisite amount of sodium is dissolved in the alcohol, and the corresponding quantity of ethyl succinate added. The mixture is refluxed for about 2 hours and then distilled, the condenser being closed by a calcium chloride tube to prevent the entrance of moisture.

25 Grams of ethyl succinate and 7 g. of sodium suffice to remove 0·5% of water from a litre of alcohol, and scarcely any loss of alcohol occurs. It is well to use approximately the above quantities even when the water present is much less than 0·5%, so that a considerable excess of the " dehydrating agents " remain, and the water is rapidly consumed. The residue can be used to dry a further smaller quantity of alcohol. An attempt has been made to estimate the amount of water in samples of this " super-dry " alcohol by the method described in the previous paper. The results, however, are indicative rather of the slight imperfections in the estimation process than of the true amount of water in this alcohol, which is too small to be estimated accurately by any known method. The mean of three such estimations was 0·01%. It is highly probable, especially in view of the enhanced hygroscopic nature of extremely dry alcohol, that the greater part of this water found its way into the alcohol during the estimation.

There remain two criticisms which may be levelled at this process for the preparation of anhydrous alcohol : (1) a certain amount of the ester may distil over with the alcohol ; (2) the ethoxide and the ester may react directly to form ethyl ether, which also would contaminate the product. These will be dealt with in turn.

It was considered unlikely that ethyl succinate would be carried over with the alcohol, owing to its high boiling point (216·5°), and a very short fractionating column was used. The alcohol, when tested, however, was found to contain 0·04 g. of ester per litre.

This impurity could probably be removed by the use of a more efficient fractionating column.

The second possibility was suggested by Cashmore, McCombie, and Scarborough (J., 1921, **119**, 970) to explain the fact that esters react with potassium ethoxide in "dry" alcohol. They state "the quantity (of ether) formed would be too small to detect." The present work renders it certain that the main reaction in their case was due to the water present in the "dry" alcohol used, since even at 70° no measurable reaction occurs after the water has disappeared. If ether were formed, of course, the titres would decrease.

This point was subjected to a more rigorous test by carrying out the reaction in concentrated solutions at 100° in sealed tubes. The titres remained constant within the limits of experimental error over a period of 11 hours. It can be safely asserted that the suggested reaction does not take place to a measurable extent, if at all, even under the above conditions, and that no ether will be formed in the dehydration of alcohol by the method described above.

From all points of view, this process is exceedingly efficient for the thorough dehydration of alcohol.

The author desires to record his appreciation of the interest which Dr. Crocker has taken in the progress of this research, and to thank the London County Council for a grant which enabled it to be undertaken.

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CLXXX.—*Acid and Salt Effects in Catalysed Reactions. Part IX. A General Kinetic Method for the Determination of the Degree of Dissociation of Water.*

By HARRY MEDFORTH DAWSON.

IN Part VIII of this series of papers (this vol., p. 1146) it was shown that the coefficients k_h and k_{OH}, which represent respectively the catalytic activities of the hydrogen and hydroxyl ions, may be derived from the reaction velocity and the hydrogen-ion concentration which are characteristic of the isocatalytic point on the H^+–OH^- catenary.

On the assumption that the catalysed hydrolytic reactions in question are such that the effect of the undissociated water molecules may be neglected, the isocatalytic data are given by the equations

$$[H^+]_i = \sqrt{k_{OH}K_w/k_h} \quad (1) \text{ and } v_i = 2\sqrt{k_h k_{OH} K_w} \quad . \quad . \quad (2)$$

If the ionisation constant, K_w, of the solvent is unknown, it is apparent that these equations afford a means of determining it. Three methods of procedure are possible, for by the combination of equations (1) and (2) we obtain

$$K_w = k_h[H^+]_i^2/k_{OH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$K_w = [H^+]_i v_i/2k_{OH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and

$$K_w = v_i^2/4k_h k_{OH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

These equations involve three of the four possible ternary combinations of k_h, k_{OH}, $[H^+]_i$, and v_i, and it should be noted that they all presume a knowledge of k_{OH}. The fourth combination (k_h, $[H^+]_i$, and v_i) does not provide a means of determining K_w, and this is due to the circumstance that these three quantities are uniquely connected by the relation $v_i = 2k_h[H^+]_i$.

In the application of the methods suggested by the above equations, it should be noted that the determination of the isocatalytic data corresponding with the joint effect of the hydrogen and hydroxyl ions usually requires the stabilisation of the p_H value at which the velocity is measured, and this may, of course, be effected by the employment of buffer mixtures. Apart from the displacement of the isocatalytic point of the H^+–OH^- catenary by the acid and salt constituents of the buffer mixture (compare Dawson, Part VIII), there are various other points to be considered which have a direct bearing on the determination of the isocatalytic data in buffered solutions, and also on the differentiation between equations (3), (4), and (5) as a means of obtaining K_w. These are of particular importance when, as is frequently the case, the products of the hydrolytic change are acidic or basic, and thus tend to alter the p_H value of the medium in which the reaction is taking place.

For the sake of simplicity it may be supposed that the catalysed reaction is the hydrolysis of an ester of the acid HA, and that the p_H value is stabilised by a mixture of HA and the corresponding salt. If x is the ratio of acid to salt in the buffer mixture, the p_H value is given by $p_H = \log 1/K - \log x$. If, further, the smallest possible change of x which permits of the measurement of the reaction velocity is denoted by Δx, it follows that $\Delta p_H/\Delta x = -1/2{\cdot}3x$, or that the resulting change in the p_H value of the solution is inversely proportional to the acid–salt ratio of the buffer mixture. This consideration shows that buffer mixtures with a low acid–salt ratio are not generally suitable for use in the measurement of reaction velocities.

Furthermore, since the rate of change of the reaction velocity with change of p_H approximates to zero in the neighbourhood of the isocatalytic point, whilst $\Delta p_H/\Delta v$ attains its highest values in this

region, it is apparent that the minimum velocity can in general be determined with much greater accuracy than that which is associated with the determination of the hydrogen-ion concentration characteristic of the isocatalytic point. For this reason, it would appear that equation (5) is very much to be preferred to equations (3) and (4) as the basis of a method for the determination of K_w.

It is scarcely necessary to add that the absolute concentration of the buffer mixture should be as small as is consistent with the adequate stabilisation of the hydrogen-ion concentration. Less obvious is the circumstance that the mode of making up the series of buffer solutions is of considerable importance. The p_H value is determined by K and by the acid–salt ratio, but of the various possible ways in which the acid and salt may be mixed together to produce a series of buffer mixtures with the required range of p_H values, there are two sets of combinations which are unique in the sense that the mathematical treatment of the catalytic relations which are associated with their use is relatively very simple. The two sets of buffer mixtures referred to are those for which (1) the concentration (c) of the acid or (2) that (s) of the salt is kept constant.

These two series of buffer mixtures give isocatalytic points, the p_H values of which are, in general, less and greater, respectively, than the corresponding p_H value for the H^+–OH^- catenary. The isocatalytic data $[H^+]_i$ and v_i for this catenary are given by equations (1) and (2). For the constant-acid series of buffer mixtures it has already been shown (Dawson, *loc. cit.*, p. 1149) that the corresponding data $[H^+]_i'$ and v_i' are given by

$$[H^+]_i' = \sqrt{(k_a Kc + k_{OH}K_w)/k_h} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and

$$v_i' = 2\sqrt{k_h(k_a Kc + k_{OH}K_w)} + k_m c \quad . \quad . \quad . \quad (7)$$

By proceeding in a similar manner, it is possible to derive expressions for the isocatalytic data $[H^+]_i''$ and v_i'' for a series of buffer solutions of the type cHA + sMA in which the salt concentration (s) is kept constant. Certain restrictions are in this case necessary, and it will be assumed that the acid is relatively weak, that the hydrogen-ion concentration is given by $[H^+] = Kc/s$, and that k_m can be neglected in comparison with k_h.

The general equation

$$v = k_h[H^+] + k_{OH}[OH^-] + k_a[A^-] + k_m[HA]$$

may then be written :

$$v = k_h[H^+] + k_{OH}K_w/[H^+] + k_a s + k_m c$$

whence

$$v = (k_h + k_m s/K)[H^+] + k_{OH}K_w/[H^+] + k_a s.$$

Differentiation of this equation shows that the reaction velocity passes through a minimum when

$$[H^+] = [H^+]_i'' = \sqrt{k_{OH}K_w/(k_h + k_m s/K)} \quad . \quad . \quad . \quad (8)$$

By substitution of this in the previous equation, we obtain :

$$v_i'' = 2\sqrt{(k_h + k_m s/K)k_{OH}K_w} + k_a s \quad . \quad . \quad . \quad (9)$$

Equations (8) and (9) express relations which are thus applicable to the isocatalytic points indicated by experiments with buffer solutions of constant salt concentration (s).

In order to illustrate the numerical differences which are involved in the use of such buffer solutions, we may compare the isocatalytic data for the acetone–iodine reaction without buffer, and the corresponding data with acetate buffers of constant-acid and of constant-salt concentration. Table I shows the values of p_H at which the reaction velocity is a minimum, the minimum ionic reaction velocity (u_i), and the minimum total velocity (v_i).

TABLE I.

Isocatalytic data with and without buffer mixtures.

Buffer mixture.	$(p_H)_i$.	u_i.	v_i.
None	4·68	1·94	1·94
Acetate buffer, $c = 0{\cdot}01$	4·33	4·38	5·88
Acetate buffer, $s = 0{\cdot}01$	4·90	1·16	5·66

It is apparent that the isocatalytic data for the two series of buffer solutions differ very widely from the data which are really characteristic of the H^+–OH^- catenary. The wide deviation in this case is due to the relatively large magnitude of the ratios k_a/k_h and k_m/k_h for the acetone–iodine reaction, and it may be anticipated that the differences in question will not be so pronounced when other hydrolytic reactions are considered.

The minimum velocity, v_i, characteristic of the H^+–OH^- catenary may be derived from the minimum velocity v_i' obtained with buffers of constant acid concentration by combining equations (2) and (7), and from the minimum velocity v_i'' observed with buffers of constant salt concentration by the combination of (3) and (9).

From (2) and (7) we obtain

$$v_i = (v_i' - k_m c)/\sqrt{(1 + k_a K c/k_{OH}K_w)} \quad . \quad . \quad . \quad (10)$$

and from (3) and (9)

$$v_i = (v_i'' - k_a s)/\sqrt{(1 + k_m s/K k_h)} \quad . \quad . \quad . \quad . \quad (11)$$

If the disturbances due to the buffer mixtures are inconsiderable, as in the case when c and s are small, it may be shown that equation (10) reduces to the form

$$v_i = v_i' - k_m c - k_a s' \quad . \quad . \quad . \quad . \quad . \quad (10A)$$

where s' is the salt concentration at which minimum velocity is observed with buffers of constant acid concentration c.

Similarly, equation (11) assumes the form

$$v_i = v_i'' - k_a s - k_m c' \quad . \quad . \quad . \quad . \quad . \quad (11A)$$

where c' represents the acid concentration at which minimum velocity is found with buffers of constant salt concentration s.

Having thus shown how the minimum reaction velocity v_i may be derived from observations made with buffered solutions, we may proceed to the derivation of K_w on the basis of equation (5).

Dissociation Constant of Water at 25°.

The experimental data employed in the calculation of K_w have reference to the rate of hydrolysis of ethyl acetate.

It will be assumed that k_h is given by the rate of hydrolysis in the presence of dilute hydrochloric acid. According to the data compiled by Schreiner (*Z. anorg. Chem.*, 1921, **116**, 102), the ratio v/c is very nearly constant for values of c between 0·025 and 0·25 mol. per litre. The value adopted here is $k_h = 6{\cdot}45 \times 10^{-3}$ (time in minutes).

Measurements by Arrhenius of the rate of saponification of ethyl acetate (*Z. physikal. Chem.*, 1887, **1**, 110) give $k_{OH} = 6{\cdot}58$ at 24·7°, which corresponds with $k_{OH} = 6{\cdot}70$ at 25°. The data obtained by Warder (*Ber.*, 1881, **14**, 1361) and Reicher (*Annalen*, 1885, **228**, 257) lead to $k_{OH} = 6{\cdot}30$ at 25°. For the purpose of this paper, the mean value, $k_{OH} = 6{\cdot}50$, is taken.

Karlsson (*Z. anorg. Chem.*, 1925, **145**, 1) has recently determined the rate of hydrolysis of the ester in acetate buffers of constant salt concentration (0·02 mol. of sodium acetate per litre), and gives for $k = 1/t \,.\, \log_{10} c_0/c$ a minimum value of $0{\cdot}24 \times 10^{-7}$. This, when multiplied by 2·30, gives $0{\cdot}55 \times 10^{-7}$, which is taken as a measure of v_i''.

The other quantities required are k_a and k_m, and these have been furnished by systematic experiments on the hydrolysis of ethyl acetate under the catalytic influence of mixtures of the series $0{\cdot}1N\text{-}CH_3{\cdot}CO_2H + xN\text{-}CH_3{\cdot}CO_2Na$. These experiments, which will be described in a later paper, give $k_a = 2{\cdot}00 \times 10^{-7}$ and $k_m = 14{\cdot}0 \times 10^{-7}$.

By substitution in equation (11) we obtain :

$$v_i = (0{\cdot}55 \times 10^{-7} - 2 \times 0{\cdot}02 \times 10^{-7}) / \sqrt{1 + (14 \times 10^{-7} \times 0{\cdot}02)/1{\cdot}85 \times 10^{-5} \times 6{\cdot}45 \times 10^{-3}}$$
$$= (0{\cdot}51/\sqrt{1{\cdot}235})10^{-7} = 0{\cdot}46 \times 10^{-7}$$

Inserting this value of v_i in equation (5) we have :

$$K_w = (0{\cdot}46 \times 10^{-7})^2/4 \times 6{\cdot}45 \times 10^{-3} \times 6{\cdot}5$$
$$= 1{\cdot}25 \times 10^{-14}.$$

The value of K_w obtained by this kinetic method depends primarily on the degree of accuracy of the measurement of v_i'' in the experiments with the buffer solutions, but there seems to be no reason why such measurements should not be made with very considerable accuracy.

It may be noted that $K_w = 1{\cdot}25 \times 10^{-14}$ is not far removed from the mean of those recorded in the Landolt–Börnstein–Roth tables. With the exception of Kanolt's value of $0{\cdot}82 \times 10^{-14}$ (*J. Amer. Chem. Soc.*, 1907, **29**, 1414), the indexed figures fall between $1{\cdot}04 \times 10^{-14}$ and $1{\cdot}42 \times 10^{-14}$. The latter values are derived on the assumptions of the classical theory, and any close comparison would necessitate a re-examination of the data from the standpoint of the modern view that the strong electrolytes are for practical purposes completely ionised.

A point of considerable interest is involved in the use of the above value of K_w for the calculation of the minimum velocity v_i from equation (2).

This gives

$$v_i = 2\sqrt{6{\cdot}45 \times 10^{-3} \times 6{\cdot}5 \times 1{\cdot}25 \times 10^{-14}} = 0{\cdot}46 \times 10^{-7}$$

which is identical with the velocity derived from equation (11). The close agreement of the observed minimum velocity when corrected for the catalytic effects of the buffer mixture with the velocity calculated from equation (2) is very significant. It would at least appear to afford substantial evidence in favour of the general accuracy of the kinetic method which has been described.

The Dissociation Constant of Water at Higher Temperatures.

In a series of experiments carried out in quartz tubes, Karlsson (*Z. anorg. Chem.*, 1921, **119**, 69) has determined the minimum rate of hydrolysis of ethyl acetate in acetate buffers of constant salt concentration (0·02 mol. per litre) at 85·5°. The minimum velocity so obtained will be utilised here for the derivation of K_w at 85·5°.

It is to be noted that the values of k_h and k_{OH} cannot be obtained by direct observations at this temperature. Within the range at which direct measurement is possible, both coefficients have been determined at a series of temperatures, and it has been shown that in both cases the influence of temperature on the velocity coefficient can be accurately represented by the Arrhenius formula

$$\log_e k'/k = A(1/T - 1/T').$$

This equation has consequently been utilised to obtain the required values of k_h and k_{OH} at 85·5°.

The value of k_h for 25°, in combination with the velocity coefficients for dilute hydrochloric acid at 20° (Poma, *Medd. Vetenskaps. Nobelinst.*, 1912, **2**, No. 11) and at 35° (Karlsson, *loc. cit.*), gives $A = 8440$, and from this the value $k_h = 0{\cdot}770$ at 85·5° is obtained.

The measurements of Warder and of Reicher (*loc. cit.*) over the range 0—40° give $A = 5578$, from which $k_{OH} = 148{\cdot}7$ at 85·5°. Karlsson's value for $k = 1/t \,.\, \log_{10} c_0/c$ is 68×10^{-7}, and this, when multiplied by 2·30, gives $v_i'' = 156 \times 10^{-7}$.

The coefficients k_a and k_m required for the buffer correction in accordance with equation (11) are not available, but as a first approximation it may be assumed that the relative effect of the buffer on the minimum velocity is the same at 85·5° as at 25°. According to this, $v_i = 46/55\ v_i'' = 0{\cdot}835\ v_i'' = 130 \times 10^{-7}$. Inserting this value of v_i in equation (5), we obtain $K_w = 37 \times 10^{-14}$.

The chief objection to the above assumption is involved in the decrease in the value of the dissociation constant K of acetic acid with rise of temperature. By interpolation from the recorded values at 25°, 100°, and 156°, we obtain $K = 1{\cdot}25 \times 10^{-5}$ at 85·5°, and when this correction is introduced, the relation between v_i and v_i'' becomes $v_i = 0{\cdot}80\ v_i''$ and the value of $K_w = 34 \times 10^{-14}$.

There are two recorded series of measurements of K_w at high temperatures with which the above value may be compared. Lorenz and Böhi (*Z. physikal. Chem.*, 1909, **66**, 733) have derived values between 0° and 100° from measurements of the *E.M.F.* of the cell 0·1*N*-HCl|0·1*N*-KCl|0·1*N*-KOH, whilst Noyes, Kato, and Sosman (*ibid.*, 1910, **73**, 1) base their values for 100°, 156°, 218°, and 306° on conductivity data obtained in connexion with the determination of the degree of hydrolysis of ammonium acetate.

Since the heat of ionisation of water varies very considerably with the temperature, the plot of log K_w against $1/T$ does not give a straight line, but the curvature of the plot is so small that there is no difficulty in estimating the value of K_w at 85·5°. For the *E.M.F.* data, the graph gives $K_w = 44 \times 10^{-14}$, whilst the hydrolytic measurements lead to $K_w = 28 \times 10^{-14}$.

The value $K_w = 34 \times 10^{-14}$ afforded by the kinetic method described in this paper thus lies between the two values which have been previously put forward. This again may be regarded as evidence in support of the belief that the determination of the minimum reaction velocity of hydrolytic reactions under the stabilised p_H conditions which are afforded by the use of buffer solutions, provides a method for the determination of the degree of dissociation of water which should yield results of considerable accuracy. With the

description and illustration of the method, the main object of this paper has been attained, and until further observations are made, it is obviously not possible to discuss in detail the merits of the kinetic method in relation to those of previous methods.

Summary.

A general kinetic method for the determination of the dissociation constant of water is described.

In accordance with the equation $K_w = v_i^2/4k_hk_{OH}$, the method involves the determination of k_h and k_{OH} and of the minimum velocity v_i, which is characteristic of the H^+–OH^- catenary.

The value of v_i is derived from measurements of the minimum reaction velocity in buffer solutions of constant acid or constant salt concentration.

For temperatures at which the coefficients k_h and k_{OH} cannot be directly measured, the required values are obtained by the use of the Arrhenius formula.

From Karlsson's measurements of the minimum speed at which ethyl acetate is hydrolysed in acetate buffers, the values derived for K_w are $1{\cdot}25 \times 10^{-14}$ at 25° and 34×10^{-14} at 85·5°.

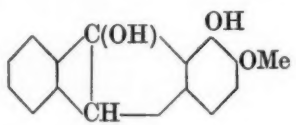
The acid and salt effects associated with the use of buffer solutions for the stabilisation of p_H in reaction velocity measurements are discussed.

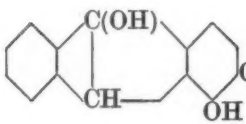
THE UNIVERSITY, LEEDS. [*Received, April 21st*, 1927.]

CLXXXI.—*Reduction Products of the Hydroxyanthraquinones. Part VIII.*

By EDWIN JOHN CROSS and ARTHUR GEORGE PERKIN.

WHEN unsymmetrical hydroxyanthraquinones are reduced to hydroxyanthranols, two isomerides can theoretically be obtained; for example, alizarin 2-methyl ether, by treatment with stannous chloride and hydrochloric acid (Miller and Perkin, J., 1925, **127**, 2684), gives both 1-hydroxy-2-methoxy- (I) and 4-hydroxy-3-

(I.) 



(II.)

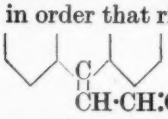
methoxy-anthranol (II), the former in larger amount. As a rule, however, only one isomeride is produced by the reduction; thus 1- and

2-hydroxyanthraquinones yield 1- and 3-hydroxyanthranols, respectively, the theoretically possible isomerides not being produced. The position of the hydroxyl in a hydroxyanthranol therefore cannot be predicted.

The positions of the hydroxyls in the anthranols of anthragallol, anthra-, and flavo-purpurins have now been studied by the method employed by one of us in earlier work and by Miller and Perkin (*loc. cit.*), *viz.*, the conversion of the hydroxyanthranol into the hydroxybenzanthrone, followed by a study of the behaviour of the product when methylated with methyl iodide and alkali. Bistrzycki and Yssel de Schepper (*Ber.*, 1898, **31**, 2790) obtained a 3 : 4 : 7-trimethoxyanthrone (which when oxidised gives flavopurpurin trimethyl ether) by the action of sulphuric acid on 4′ : 5 : 6-trimethoxydiphenylmethanecarboxylic acid, but there is no evidence that this is a methylation product of the hydroxyanthranol derived from flavopurpurin itself (Liebermann, *Ber.*, 1888, **21**, 435).

A drawback to the application of the benzanthrone process (employing glycerol and sulphuric acid) to the hydroxyanthranols is that these are more or less decomposed by the sulphuric acid before the desired reaction occurs, and so the yield of hydroxybenzanthrone is sometimes very small or even infinitesimal. The replacement of sulphuric acid by potassium hydrogen sulphate is sometimes effective. As a rule, more certain results can be obtained by passing hydrogen chloride through a mixture of the hydroxyanthranol and acraldehyde in acetic acid solution. For example, although hydroxybenzanthrones could be prepared in satisfactory amount from the anthranols of anthrapurpurin and anthragallol by all three methods, the acraldehyde method alone was successful in the conversion of flavopurpurin-anthranol into the trihydroxybenzanthrone. 3-Hydroxyanthranol thus gives 2-hydroxybenzanthrone. By this method, however, benzalizarin could not be obtained from 3 : 4-dihydroxy(alizarin)-anthranol.

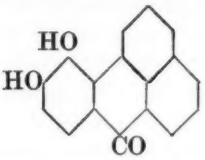
The preparation of hydroxybenzanthrone derivatives by the direct action of acraldehyde in this manner is interesting, because in order that ring formation may take place from the allylanthranol,

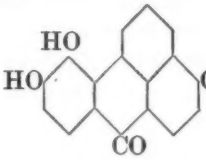


, which is evidently the first product of the reaction, an oxidising agent is necessary. This is presumably supplied by the excess of acraldehyde present, which, as the result, is reduced to allyl alcohol.

The hydroxybenzanthrone, $C_{17}H_{10}O_4$, derived from anthrapurpurin-anthranol closely resembles benzalizarin (III) in properties. Since it yields a *triacetyl* derivative on acetylation, and with methyl

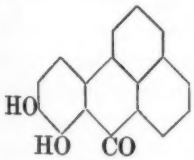
iodide and alkali in theoretical amount a *trimethyl ether*, it is evidently the 2 : 7 : 8-trihydroxy-compound (IV).

(III.) 

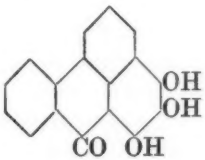


(IV.)

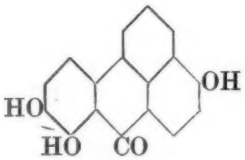
This substance, which we have named *benzanthrapurpurin*, gives a crimson oxonium salt, $C_{17}H_{10}O_4,H_2SO_4$, and dyes shades similar to, although slightly yellower than, those given by anthrapurpurin itself. On the other hand, iso*benzanthragallol*, $C_{17}H_{10}O_4$, obtained in a similar manner from anthragallol-anthranol, crystallises in yellow needles and differs markedly from anthragallol in properties. On acetylation, a *diacetyl* compound only is obtained, and the substance is not methylated by treatment with methyl iodide or with methyl sulphate and alkali. With diazomethane, however, a *dimethyl ether* is produced. This is unattacked by prolonged boiling with acetic anhydride and pyridine, but gives with alcoholic potash a *potassium* salt, and it is thus evident that of the three hydroxyls present in this compound one, evidently adjacent to a carbonyl group, is remarkably resistant both to methylation and to acetylation. A somewhat similar difficulty was experienced in the case of *iso*benzalizarin (V) (*loc. cit.*). *iso*Benzanthragallol is consequently either a 2 : 3 : 4- (VI) or a 5 : 6 : 7-trihydroxybenzanthrone. For reasons given later, the first of these constitutions appears to be preferable.



(V.)



(VI.)



(VII.)

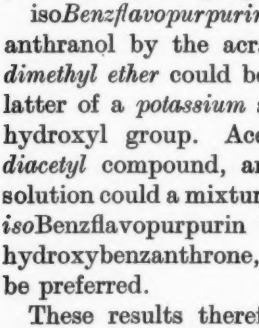
The substance dyes shades distinct from and weaker than those given by anthragallol.

Crude deoxyflavopurpurin from commercial flavopurpurin gives an amorphous acetyl derivative (compare Liebermann, *loc. cit.*; Graebe and Thode, and Bernhard, *Annalen*, 1906, **349**, 207, 222), and cannot be purified in the same way as anthrapurpurin-anthranol (Goodall and Perkin, J., 1924, **125**, 470). A crystalline acetyl compound of the pure substance has also not been described. It is now found that if crude flavopurpurin, crystallised from nitrobenzene, is reduced to the anthranol, and the product is partly

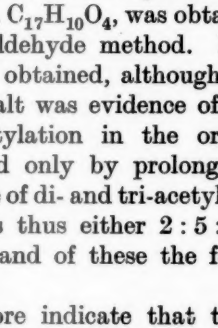
acetylated in the cold, a crude *diacetyl* derivative is obtained which can be freed by recrystallisation from the acetyldeoxyanthraflavic acid which is present. The pure diacetyl compound thus obtained is converted by Fischer and Bergmann's method of acetylation (*Ber.*, 1918, **51**, 1797) into *tetra-acetyldeoxyflavopurpurin*, which is readily obtained pure in pale yellow plates. Hydrolysis of this yields deoxyflavopurpurin, which crystallises in deep yellow plates.

iso*Benzflavopurpurin*, $C_{17}H_{10}O_4$, was obtained from flavopurpurin-anthranol by the acraldehyde method. By methylation, only a *dimethyl ether* could be obtained, although the formation from the latter of a *potassium* salt was evidence of the presence of a third hydroxyl group. Acetylation in the ordinary manner gave a *diacetyl* compound, and only by prolonged treatment in boiling solution could a mixture of di- and tri-acetyl derivatives be produced. *iso*Benzflavopurpurin is thus either 2 : 5 : 6- (VII) or 3 : 4 : 7-trihydroxybenzanthrone, and of these the former constitution is to be preferred.

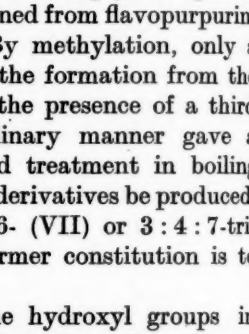
These results therefore indicate that the hydroxyl groups in anthrapurpurin-, anthragallol-, and flavopurpurin-anthranols are present respectively in the 3 : 4 : 6 (VIII), 1 : 2 : 3 (IX), and 1 : 2 : 6 (X) positions.



(VIII.)



(IX.)



(X.)

Miller and Perkin (*loc. cit.*) suggested that the reduction of a hydroxyanthraquinone to its anthranol or anthrone will take place in such a way that any β-hydroxyl in the former will preferably occupy a para-position with respect to the anthranol hydroxyl (9) or anthrone carbonyl group in the latter. Although the conditions dealt with in the present communication differ from those discussed on the former occasion, because two β-hydroxyls are present in all the hydroxyanthraquinones now studied, it will be observed, on examining the formulæ of the hydroxyanthranols given above, that this suggestion still holds good in the case of one β-hydroxyl group at least. The presence of such a hydroxyl in a hydroxyanthraquinone seems, therefore, to be a determining factor in the orientation of the hydroxyls of the anthranol derived from it by reduction. Moreover, it is now suggested as likely that in all cases where the β-hydroxyl is present in the anthranol in the 3- or 6-position, and the contiguous α-position is free, the benz-

anthrone condensation will take place at the latter point; for instance, 3-hydroxyanthranol gives 2-hydroxybenzanthrone, and anthrapurpurin(3 : 4 : 6-trihydroxy)-anthranol gives 2 : 7 : 8-trihydroxybenzanthrone. It is therefore considered probable that the trihydroxybenzanthrones derived from anthragallol- (IX) and flavopurpurin- (X) anthranols will be represented by the formulæ (VI) and (VII).

Interesting again is the fact that 3-hydroxyanthranol, on treatment with alkali and glucose (Bradshaw and Perkin, J., 1922, **121**, 911), yields 2-hydroxybenzanthronecarboxylic acid.

Benzalizarin (III) and benzanthrapurpurin (IV) are red substances and their dyeing properties resemble those of alizarin and anthrapurpurin, respectively. *iso*Benzflavopurpurin (VII) dyes yellow shades of a similar character to those of *iso*benzalizarin (V) and differs markedly from flavopurpurin in this respect. According to the quinonoid theory, (III) and (IV) can only be represented as *p*-quinonoid and (V) and (VII) as *o*-quinonoid dyes, and, as suggested in a previous communication (*loc. cit.*), the very distinct shades of red and yellow given by these colouring matters respectively are explainable on the assumption that they possess such configurations. On the other hand, *iso*benzanthragallol (VI), as its formula suggests, may be represented as either a *p*- or an *o*-quinonoid dye, though its somewhat feeble tinctorial property favours the latter view.

Experimental.

Benzanthrapurpurin.—A mixture of anthrapurpurin-anthranol (4 g.; prepared by hydrolysis of pure acetylanthrapurpurin-anthranol: Goodall and Perkin, *loc. cit.*), sulphuric acid (47 c.c.), water (23 c.c.), and glycerol (8 g.) was slowly heated to 125—130° with constant stirring and kept at that temperature for 1 hour. The dark red solution, when cold, was poured into water, the precipitate was collected, washed, dried, and repeatedly extracted with boiling alcohol, and the extracts were concentrated and poured into much ether. The solution was filtered, well washed, and evaporated, and the dark brown residue (3·1 g.) was digested with acetic anhydride and a trace of pyridine. The product, after repeated crystallisation from acetic acid (charcoal), was obtained in yellow plates (1·9 g.), m. p. 245—246° (Found: C, 68·3; H, 4·2; $C_2H_4O_2$, 44·7. $C_{23}H_{16}O_7$ requires C, 68·3; H, 4·0; $C_2H_4O_2$, 44·55%).

This compound, evidently *triacetylbenzanthrapurpurin*, gave with sulphuric acid a deep red solution, which gradually deposited crimson, microscopic needles of *benzanthrapurpurin sulphate*. These were collected, washed with glacial acetic acid, and dried

at 100° (Found: $C_{17}H_{10}O_4$, 73·75. $C_{17}H_{10}O_4,H_2SO_4$ requires $C_{17}H_{10}O_4$, 73·9%).

The *benzanthrapurpurin* obtained from this salt by the action of boiling water crystallised from dilute alcohol in microscopic, orange needles which did not melt below 340° and dissolved in caustic soda solution with a violet coloration. It produced light brown, orange, dull maroon, and dark brown shades on wool mordanted with aluminium, tin, chromium, and iron respectively.

Methylation. To a boiling mixture of acetylbenzanthrapurpurin (2 g.), methyl alcohol (30 c.c.), and methyl iodide (12 c.c.), a solution of caustic potash (2 g.*) in methyl alcohol was gradually added during 12 hours. The excess of methyl iodide was distilled off, the deep reddish-brown liquid was kept over-night, and the crystals that separated were washed with water and dried. The light brown product (0·98 g.) was dissolved in benzene, and a small amount of alcoholic potash added to precipitate any dimethyl ether present as potassium salt. The filtered and concentrated solution deposited crystals over-night, which, by recrystallisation from benzene (charcoal), were obtained in golden-yellow needles (0·45 g.), m. p. 185—185·5° (Found: C, 74·9; H, 4·9; CH_3, 13·7. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0; CH_3, 14·1%).

This compound, *benzanthrapurpurin trimethyl ether*, could also be obtained by methylating benzanthrapurpurin with methyl sulphate in the usual manner.

To demethylate this compound completely, it was necessary to perform the Zeisel determination twice on the same material, as was the case with benzalizarin dimethyl ether (Perkin, J., 1920, **117**, 696).

iso*Benzanthragallol.*—A mixture of anthragallol-anthranol (2 g.), glycerol (50 g.), and powdered anhydrous potassium hydrogen sulphate (20 g.), made into a smooth paste, was gradually heated, with stirring, to 190—200°; the solution was maintained at this temperature for ½ hour, a light brown powder separating. The mixture was cooled somewhat and poured into water, and the precipitate thus produced was washed by decantation, dried, and extracted two or three times with cold alcohol to remove resinous impurities. The product was acetylated, and the crystals that separated (0·9 g.) were recrystallised repeatedly from acetic acid, giving yellow needles of *diacetyl*iso*benzanthragallol*, m. p. 232—233° (Found: C, 69·5; H, 4·0; $C_2H_4O_2$, 32·75. $C_{21}H_{14}O_6$ requires C, 69·6; H, 3·9; $C_2H_4O_2$, 33·15%).

This diacetyl compound, when hydrolysed with hydrochloric

* Commercial stick. Theory requires 1·66 g. KOH for hydrolysis and methylation.

and acetic acids, gave 77·06% of iso*benzanthragallol* (calc., 76·8%). The latter crystallised from nitrobenzene in yellow needles, m. p. 319—321° (decomp.), sparingly soluble in alcohol, ether, benzene, or acetic acid (Found : C, 73·3; H, 3·8. $C_{17}H_{10}O_4$ requires C, 73·4; H, 3·6%).

*iso*Benzanthragallol becomes blood-red, without apparently dissolving, on treatment with caustic soda solution, and dyes mordanted woollen cloth shades which are distinct from those given by anthragallol. Pale brown, yellow, light brown, and olive shades are obtained on aluminium, tin, chromium, and iron mordants, respectively.

By prolonged digestion (27 hours) with acetic anhydride and a trace of pyridine, the diacetyl derivative only could be obtained. Acetylation in the cold by Fischer and Bergmann's method (*loc. cit.*) yielded, at least mainly, the diacetyl derivative, without apparent solution of the *iso*benzanthragallol.

iso*Benzanthragallol Dimethyl Ether*.—As experiment showed that methylation of *iso*benzanthragallol could not be effected with methyl iodide or methyl sulphate in the usual way, a suspension of *iso*benzanthragallol (1·5 g.) in dry ether (120 c.c.) was treated with diazomethane (generated from 6 c.c. of nitrosomethylurethane) and kept over-night. The excess of diazomethane was then removed, the solution filtered from unchanged *iso*benzanthragallol (0·8 g.), the filtrate evaporated to dryness, and the residue washed with a little acetone to remove resinous matter. There was thus obtained a yellow, crystalline powder (0·22 g.), and a further small amount (0·03 g.) was deposited from the acetone washings after concentration. By repeated crystallisation from benzene (animal charcoal), yellow needles of iso*benzanthragallol dimethyl ether*, m. p. 152—153°, were obtained (Found : C, 74·5; H, 4·7; CH_3, 9·8. $C_{19}H_{14}O_4$ requires C, 74·5; H, 4·6; CH_3, 9·8%). The final acetone filtrate contained much resinous matter from which nothing definite could be isolated.

In the Zeisel determination, it was found necessary to submit the substance to a second distillation with hydriodic acid. The residue, after treatment with bisulphite solution, consisted of *iso*benzanthragallol.

*iso*Benzanthragallol dimethyl ether did not yield an acetyl derivative even by prolonged digestion (5 hours) with acetic anhydride and pyridine. It was soluble with difficulty in absolute alcohol, yielding a faintly yellow solution which, on the addition of alcoholic potash, became of a somewhat deeper colour. On keeping, pale yellow, hair-like, silky needles separated which were washed with alcohol and dried. They darkened at 130°, melted at 235—240°

to form a black liquid, gave ash on ignition, and evidently consisted of the monopotassium salt of *iso*benzanthragallol dimethyl ether. A suspension in absolute alcohol to which a trace of phenolphthalein was added showed no red coloration, but on addition of water this was observed owing to decomposition of the potassium salt.

Methylation. To a boiling suspension of *iso*benzanthragallol dimethyl ether (0·5 g.) in methyl alcohol (10 c.c.) and methyl iodide (3 c.c.), a solution of caustic potash (0·12 g.*) in methyl alcohol was gradually added during 11 hours, and the digestion was continued for 2—3 hours longer. The excess of methyl iodide was removed, and after 12 hours the crystals were collected, washed with methyl alcohol and with water, and dried. The yellow, microscopic needles (0·45 g.), m. p. 152—153°, were shown to consist entirely of unchanged *iso*benzanthragallol dimethyl ether by a mixed m.-p. determination.

Flavopurpurin-anthranol.—Commercial flavopurpurin (10 g.), partly purified by crystallisation from nitrobenzene, was treated for 1 hour with a boiling solution of stannous chloride (10 parts) in hydrochloric acid (50 parts). When cold, the product was collected, washed with hydrochloric acid and with water, and dried. The light brown powder (8·7 g.), on treatment with acetic anhydride and potassium acetate in the cold, slowly dissolved, but after a short time crystals separated; after 12 hours, these were collected and washed with alcohol (yield, 4·3 g.). By repeated crystallisation from acetic acid (charcoal), this *acetyl* derivative was obtained in yellow plates (2·2 g.), m. p. 209—212° (Found: C, 66·2; H, 4·4; $C_2H_4O_2$, 36·6. $C_{18}H_{14}O_6$ requires C, 66·25; H, 4·3; $C_2H_4O_2$, 36·8%).

This substance, *diacetylflavopurpurin-anthranol*, was hydrolysed with hydrochloric acid in acetic acid solution in the usual way. The product, by recrystallisation from dilute alcohol, was obtained in deep yellow, rectangular plates which darkened at 200° and melted at 231—233° when slowly heated. If the m.-p. tube, however, was introduced into a bath at 235°, the substance melted at 243—245° (Found: C, 69·4; H, 4·3. Calc. for $C_{14}H_{10}O_4$: C, 69·4; H, 4·1%). Graebe and Thode (*loc. cit.*) described it as a crystalline powder, m. p. 258°. Flavopurpurin-anthranol dissolves in caustic soda solution with an orange-red colour which in air rapidly develops the purple tint characteristic of the alkaline solution of flavopurpurin.

By acetylating diacetylflavopurpurin-anthranol by Fischer and Bergmann's method (*loc. cit.*), *tetra-acetylflavopurpurin-anthranol*

* Commercial stick. Theory requires 0·09 g. KOH.

was obtained, which, after repeated crystallisation from methyl alcohol, was isolated in very pale yellow, rectangular plates, m. p. 181—182°, sparingly soluble in methyl alcohol with formation of a blue fluorescent solution (Found: C, 64·2; H, 4·5; $C_2H_4O_2$, 58·3. $C_{22}H_{18}O_8$ requires C, 64·4; H, 4·4; $C_2H_4O_2$, 58·5%).

Tetra-acetylflavopurpurin-anthranol, on oxidation with chromic acid in acetic acid solution, gave yellow needles of triacetylflavopurpurin, m. p. 208—211° (Frobenius and Hepp, *Ber.*, 1907, **40**, 1049, give m. p. 202—203°).

iso*Benzflavopurpurin*.—Attempts to prepare this substance by the glycerol–sulphuric acid method were unsuccessful, and the following procedure was therefore adopted. Hydrogen chloride was passed into a mixture of diacetylflavopurpurin-anthranol (1 g.), acraldehyde (3 c.c. of a solution of 1 part of acraldehyde in 5 parts of glacial acetic acid), and glacial acetic acid (10 c.c.), and the mixture was heated to the b. p. during ¼ hour and boiled for ¼ hour. The yellow solution became orange as the boiling point was reached, and brown at the end of the operation. The solution, poured into boiling water (150 c.c.), gave a resinous precipitate. This, which solidified when cold, was ground with water, washed, and digested with boiling acetic anhydride and a trace of pyridine. The crystals (0·4 g.) of *diacetyliso*benzflavopurpurin thus obtained separated from acetic acid (charcoal) in yellow needles (0·23 g.), which sintered at 233° and melted at 236° (Found: C, 69·4; H, 3·9; $C_2H_4O_2$, 33·01. $C_{21}H_{14}O_6$ requires C, 69·6; H, 3·9; $C_2H_4O_2$, 33·15%).

Benzanthrapurpurin, *iso*benzanthragallol, and 2-hydroxybenzanthrone, prepared in about 30% yield from anthrapurpurin- and anthragallol-anthranols and 3-hydroxyanthranol, respectively, by this acraldehyde method, were identified by the melting points of their acetyl derivatives.

Diacetyl*iso*benzflavopurpurin, hydrolysed with hydrochloric acid in presence of acetic acid, gave iso*benzflavopurpurin*, which is soluble in alkaline solutions with a yellow colour. It is sparingly soluble in acetic acid, and crystallises therefrom in long, light brown needles containing one molecule of acetic acid of crystallisation (Found: $C_{17}H_{10}O_4$, 82·1. $C_{17}H_{10}O_4+C_2H_4O_2$ requires $C_{17}H_{10}O_4$, 82·25%). These crystals, although stable at 100°, are converted at 160° with loss of acetic acid into dull yellow needles, m. p. 293—295° (decomp.) (Found: C, 73·2; H, 3·7. $C_{17}H_{10}O_4$ requires C, 73·4; H, 3·6%).

*iso*Benzflavopurpurin dyes shades which are quite distinct from those yielded by flavopurpurin. On wool mordanted with aluminium, tin, chromium, and iron, yellow, pale yellow, yellowish-brown, and brown shades are respectively obtained.

By treatment for 5 hours with boiling acetic anhydride and

pyridine, *iso*benzflavopurpurin gave a product which melted at 217—221° and consisted of yellow needles, probably of the triacetyl derivative, mixed with clusters of microscopic needles of the diacetyl compound. Even after further prolonged boiling, some diacetyl derivative still remained.

Methylation. A mixture of diacetyl*iso*benzflavopurpurin (1 g.), methyl alcohol (15 c.c.), and methyl iodide (6 c.c.) was boiled for 16 hours, a solution of caustic potash (0·9 g.*) in methyl alcohol being gradually added. From the clear solution at first obtained, a yellow precipitate of the potassium compound of the methyl ether slowly separated, and this was collected, washed with water, and dried. This compound, which did not melt below 300° and gave an ash on ignition, was ground with dilute hydrochloric acid (1 : 4), the mixture boiled, and the precipitate collected (yield, 0·65 g.). The product, now ash-free, crystallised from alcohol–acetic acid in long, light brown needles, m. p. 199—200° (Found : C, 74·3; H, 4·8; CH_3, 9·7. $C_{19}H_{14}O_4$ requires C, 74·5; H, 4·6; CH_3, 9·8%).

iso*Benzflavopurpurin dimethyl ether* was completely demethylated only after the finely divided substance had been boiled with hydriodic acid for 12 hours.

A solution of the dimethyl ether in absolute alcohol, on addition of alcoholic potash, gave an immediate crystalline precipitate of the monopotassium salt.

We are much indebted to the British Alizarine Co., Ltd., for the commercial anthra- and flavo-purpurin necessary for this investigation.

CLOTHWORKERS RESEARCH LABORATORY,
THE UNIVERSITY, LEEDS. [*Received, March 29th*, 1927.]

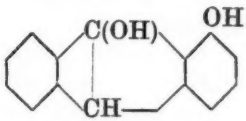
CLXXXII.—*Reduction Products of the Hydroxyanthraquinones. Part IX.*

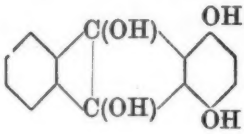
By ALEXANDER MACMASTER and ARTHUR GEORGE PERKIN.

THE aluminium–mercury couple, by means of which 2-mono- and 2 : 6-, 2 : 7-, and 1 : 2-di-hydroxyanthracenes were readily obtained from the corresponding hydroxyanthraquinones or their anthranols, and also anthracene from anthraquinone (Hall and Perkin, J., 1923, **123**, 2029), reduces 1-mono-, 1 : 5-di-, and 1 : 2 : 3- and 1 : 2 : 6-tri-hydroxyanthraquinones, not to the hydroxyanthracenes, but

* Commercial stick. Theory requires 0·77 g. KOH for hydrolysis and methylation.

only to the hydroxyanthranols. The stability of these hydroxyanthranols is thus evidently due to the effect of one or other of the hydroxyls present therein, and these it is now known occupy the 1-, 1 : 5-, 1 : 2 : 3-, and 1 : 2 : 6-positions, respectively (Cross and Perkin, preceding paper). There is evidence that in compounds

(I.) 



(II.)

of this type a residual affinity exists between the hydroxyls in positions 1 and 9, as, for instance, in quinizarin, which is reduced by stannous chloride and hydrochloric acid merely to *leuco*-quinizarin (II) and not further to the hydroxyanthranol. The resistance of 1-hydroxyanthranol (I) to reduction by the aluminium–mercury couple also harmonises with this view, but, on the other hand, there are cases where a somewhat similar behaviour is observed with substances of this type in which the 1-hydroxyl is absent. For example, though 3 : 4-dihydroxy(alizarin)-anthranol, on treatment with the couple, readily yields 1 : 2-dihydroxyanthracene, 3 : 4 : 6-trihydroxy(anthrapurpurin)-anthranol gives but traces of a reduction product, which has not yet been isolated pure. As a means of overcoming this difficulty, a preliminary methylation of the hydroxyanthraquinones or their anthranols suggested itself; indeed Ladgozinski (*Annalen*, 1905, **342**, 104) has shown that hystazarin dimethyl ether is readily reduced to 2 : 3-dimethoxyanthracene even with zinc dust and ammonia. There should be, however, no difficulty in preparing 2 : 3-dihydroxyanthracene from hystazarin itself by the aid of the aluminium–mercury couple. The present communication deals with anthrapurpurin trimethyl ether, and this has been converted, by long digestion in alcoholic solution with the couple in presence of ammonia, into 1 : 2 : 7-trimethoxyanthracene in moderate yield. For the preparation of anthrapurpurin trimethyl ether, the method of Graebe and Bernhard (*Annalen*, 1906, **349**, 222) was employed, that is, 3 : 4 : 6-trihydroxyanthranol was methylated and then oxidised with chromic acid. The methylated anthranol, which was not closely examined by those authors, is the 3 : 4 : 6 : 9-tetramethoxy-compound, and this is interesting because the analogous product from deoxyalizarin (3 : 4-dihydroxyanthranol) is 3 : 4-dimethoxyanthrone (Graebe and Thode, *Annalen*, 1906, **349**, 207). In addition to the tetramethoxy-compound, some 3 : 4 : 6-trimethoxyanthranol was produced, a compound which is more readily obtained by the reduction of anthrapurpurin trimethyl

ether in acetic acid solution with stannous chloride and hydrochloric acid. This with acetic anhydride and pyridine yields the 3 : 4 : 6-trimethoxy-9-acetyl compound. Finally, if air is not excluded during the methylation process, a small amount of 3 : 4 : 6 : 3′ : 4′ : 6′-hexamethoxydianthrone is formed. This can also be prepared by the oxidation of 3 : 4 : 6-trimethoxyanthranol with ferric chloride in presence of acetic acid.

EXPERIMENTAL.

3 : 4 : 6-Trihydroxyanthranol was obtained from commercial anthrapurpurin by reduction with stannous chloride and hydrochloric acid (Goodall and Perkin, J., 1924, **125**, 470), and the acetylated product was crystallised from alcohol–acetic acid until it was free from acetyl*iso*anthraflavic acid anthranol. To a suspension of the product (10 g.) in boiling 80% methyl alcohol (300 c.c.), potassium hydroxide (50 g. in 50 c.c. of water) and methyl sulphate (55 c.c.) were slowly added through capillary tubes attached to the condenser; the mixture was kept slightly alkaline, and access of air was prevented as far as possible. The liquid, after being acidified, slowly deposited crystals, which were washed with dilute alkali solution and dried over sulphuric acid. The pale brown product (yield, 60%) was repeatedly extracted with boiling ligroin (200 c.c.). The extract after concentration deposited pale yellow needles which melted at 107° after recrystallisation (yield, 40%) (Found: C, 72·4; H, 6·0; CH_3, 20·0. $C_{18}H_{18}O_4$ requires C, 72·4; H, 6·0; CH_3, 20·0%). 3 : 4 : 6 : 9-*Tetramethoxyanthranol* gives green, fluorescent solutions, and dissolves in sulphuric acid with a brown colour which changes to purple on addition of a trace of nitric acid. That portion of the methylation product insoluble in ligroin contained, in addition to anthrapurpurin trimethyl ether, a small amount of 3 : 4 : 6-trimethoxyanthrone, a compound described later.

3 : 4 : 6 : 9-Tetramethoxyanthranol (9·5 g.) was oxidised in boiling acetic acid (65 c.c.) with a solution of chromic acid (7 g.) in acetic acid (10 c.c.) and water (15 c.c.). When cold, the anthrapurpurin trimethyl ether was collected and recrystallised from benzene. It melted at 198° (Graebe and Bernhard, *loc. cit.*, give m. p. 201°).

1 : 2 : 7-*Trimethoxyanthracene.*—A solution of anthrapurpurin trimethyl ether (4 g.) in cold sulphuric acid was poured into water, and the precipitate was collected and added in the moist condition to alcohol (100 c.c.). The suspension was boiled and treated with the aluminium–mercury couple (0·5 g.) and concentrated ammonia solution (6 c.c.), these additions being repeated five times during

4 hours. The blue, fluorescent solution, acidified with hydrochloric acid and evaporated to one-fourth of its bulk, deposited crystals (2·2 g.), which were washed with dilute alkali solution and recrystallised from ligroin (yield, 1·8 g.) (Found: C, 75·8; H, 5·9; CH_3, 16·3. $C_{17}H_{16}O_3$ requires C, 75·55; H, 5·9; CH_3, 16·7%). 1 : 2 : 7-*Trimethoxyanthracene* forms prismatic needles which melt at 95° and are very soluble in the usual solvents. Its solutions in benzene and alcohol are fluorescent. The solution in sulphuric acid is orange-yellow, but on gentle heating becomes a plum-coloured liquid with a green fluorescence, a type of colour change common to the hydroxyanthracenes (Hall and Perkin, *loc. cit.*, p. 2032).

3 : 4 : 6-*Trimethoxyanthranol.*—To a boiling solution of stannous chloride (10 g.) in hydrochloric acid (25 c.c.), anthrapurpurin trimethyl ether (1 g.), dissolved in acetic acid (30 c.c.), was added, and the digestion continued for 1 hour. The liquid, diluted with hot hydrochloric acid, deposited canary-yellow crystals, which became almost colourless after washing (yield, 0·9 g.) and were obtained in needles, m. p. 149°, by recrystallisation from alcohol (Found: C, 71·85; H, 5·5; CH_3, 15·4. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6; CH_3, 15·8%). 9-*Acetyl*-3 : 4 : 6-*trimethoxyanthranol*, obtained by acetylation in the usual manner, formed colourless needles, m. p. 127° (Found: $C_2H_4O_2$, 13·9. $C_{19}H_{18}O_5$ requires $C_2H_4O_2$, 13·2%).

3 : 4 : 6 : 3′ : 4′ : 6′-*Hexamethoxydianthrone.*—A solution of 3 : 4 : 6-trimethoxyanthranol (7 g.) in acetic acid (25 c.c.) was treated with commercial ferric chloride (10 g.) in acetic acid (10 c.c.) and gently boiled for 2 hours. When cold, the crystals were collected, washed with alcohol, and recrystallised from alcohol–acetic acid (Found: C, 72·3; H, 5·2; CH_3, 15·6. $C_{34}H_{30}O_8$ requires C, 72·1; H, 5·3; CH_3, 15·9%). The *hexamethoxy*-compound forms colourless needles which are very sparingly soluble in alcohol, melt at 224°, and dissolve in sulphuric acid with a yellow colour which becomes purple on heating. It does not appear to enolise readily and does not pass into the acetyldianthranol when digested with boiling acetic anhydride and pyridine. Attempts to convert this compound into the corresponding dianthraquinone and helianthrone have as yet been unsuccessful.

Our thanks are due to the British Alizarine Co., Ltd., for the commercial anthrapurpurin employed in this investigation.

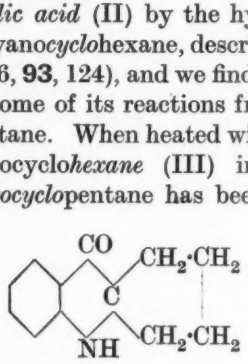
CLOTHWORKERS RESEARCH LABORATORY,
THE UNIVERSITY, LEEDS. [*Received, March 29th*, 1927.]

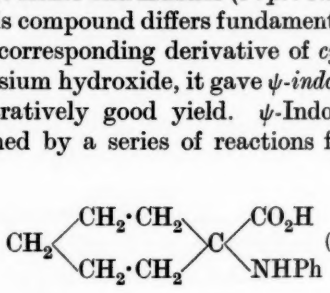
CLXXXIII.—*The Reactions of* 1-*Anilino*cyclo*hexane*-1-*carboxylic Acid. Synthesis of* ψ-*Indoxyl*spirocyclo*hexane.*

By Raymond Livingston Betts, Rudolph Muspratt, and Sydney Glenn Preston Plant.

It was shown by Plant and Facer (J., 1925, **127**, 2037) that the fusion of 1-anilino*cyclo*pentane-1-carboxylic acid with a mixture of potassium hydroxide and sodium ethoxide, under conditions similar to those used by Bucherer and Grolée (*Ber.*, 1906, **39**, 986) for the preparation of 2 : 2-dimethyl-ψ-indoxyl from α-anilino*iso*butyric acid, yielded carbazole and not the expected ψ-indoxyl*spirocyclo*pentane (I). We have now prepared 1-*anilino*cyclo*hexane*-1-*carboxylic acid* (II) by the hydrolysis, first to the *amide*, of 1-anilino-1-cyano*cyclo*hexane, described by Walther and Hübner (*J. pr. Chem.*, 1916, **93**, 124), and we find that this compound differs fundamentally in some of its reactions from the corresponding derivative of *cyclo*pentane. When heated with potassium hydroxide, it gave ψ-*indoxyl*spirocyclo*hexane* (III) in comparatively good yield. ψ-Indoxyl-*spirocyclo*pentane has been obtained by a series of reactions from

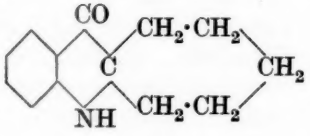
(I.)





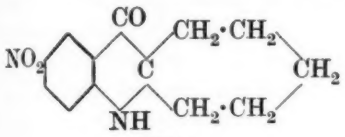
(II.)

(III.)

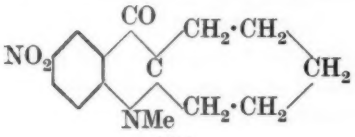


tetrahydrocarbazole (Perkin and Plant, J., 1923, **123**, 676) and, owing to the fact that it gives a number of interesting derivatives, including co-ordinated compounds of the alkali metals (Sidgwick and Plant, J., 1925, **127**, 209), it was hoped to obtain confirmatory evidence for its structure by synthesis from 1-anilino*cyclo*pentane-1-carboxylic acid by the method mentioned above. Although this led to other results, we now find that the reactions of ψ-indoxyl-*spirocyclo*hexane are so similar to those observed with ψ-indoxyl-*spirocyclo*pentane that they amply confirm the structure assigned to the latter compound. ψ-Indoxyl*spirocyclo*hexane can be acetylated, and is easily nitrated by dilute nitric acid to give 10-*nitro*-ψ-*indoxyl*spirocyclo*hexane* (IV), which gives a character-

istic sodium derivative, from which 10-*nitro*-7-*methyl*-ψ-*indoxyl*-spirocyclo*hexane* (V) can readily be obtained. The conditions required for these reactions and the characteristic properties of the



(IV.)



(V.)

products are exactly those observed in the corresponding *cyclo*pentane series. Like ψ-indoxyl*spirocyclo*pentane, ψ-indoxyl-*spirocyclo*hexane could not be made to give a nitroso-derivative or a semicarbazone. The behaviour of these two compounds towards sodium hydroxide is fundamentally similar. Only on heating with concentrated aqueous sodium hydroxide is a metallic derivative obtained, and, in both cases, water instantaneously brings about hydrolysis of the product, but whilst the sodium derivative of ψ-indoxyl*spirocyclo*pentane can be obtained with a second molecule of ψ-indoxyl*spirocyclo*pentane attached to it by co-ordinate links, similar conditions gave only the simple sodium salt of ψ-indoxyl*spirocyclo*hexane. There is here no fundamental difference between the two compounds, since the isolation of these co-ordinated compounds in this series must depend upon a number of arbitrary factors, such as the melting point.

It has been shown (Plant and Facer, *loc. cit.*) that 1-anilino*cyclo*pentane-1-carboxylic acid, on heating, loses aniline and water to give the lactone of 1-1′-hydroxy*cyclo*pentane-1′-carboxylylanilino-*cyclo*pentane-1-carboxylic acid. 1-Anilino*cyclo*hexane-1-carboxylic acid does not appear to undergo this reaction, but breaks up into aniline and Δ^1-*cyclo*hexene-1-carboxylic acid.

EXPERIMENTAL.

1-*Anilino*cyclo*hexane*-1-*carboxylic Acid* (II).—1-Anilino-1-cyano-*cyclo*hexane was prepared by Walther and Hübner's method (*loc. cit.*). The *nitrosoamine* separated when its solution in alcohol containing hydrochloric acid was treated with concentrated aqueous sodium nitrite, and, after recrystallisation from methyl alcohol, it was obtained in pale yellow prisms, m. p. 70°. When a solution of 1-anilino-1-cyano*cyclo*hexane in concentrated sulphuric acid was kept for 2 days at room temperature and then poured on ice, and the mixture was made alkaline with ammonia, 1-*anilino*cyclo*hexane*-1-*carboxylamide* separated quantitatively in a pure condition. It crystallised from dilute alcohol in colourless plates, m. p. 148°

(Found: N, 12·4. $C_{13}H_{18}ON_2$ requires N, 12·8%). The *nitrosoamine* separated from methyl alcohol in pale yellow prisms, m. p. 172°. This amide was comparatively stable and hydrolysis to the corresponding acid was complete only after prolonged boiling with hydrochloric acid. On rubbing with concentrated hydrochloric acid, the *hydrochloride* of the amide separated; a paste of this was added to an excess of hydrochloric acid, and the mixture was boiled under reflux with continuous stirring for 12 hours and then evaporated to dryness. The residue was heated with an excess of dilute aqueous sodium hydroxide, and the solution was filtered and acidified with glacial acetic acid; 1-*anilino*cyclo*hexane*-1-*carboxylic acid* then separated. After recrystallisation from alcohol, it was obtained in colourless prisms, m. p. 142° (Found: N, 6·2. $C_{13}H_{17}O_2N$ requires N, 6·3%).

1-Anilino*cyclo*hexane-1-carboxylic acid was heated in a distillation flask, and the oily distillate treated with an excess of dilute hydrochloric acid; the undissolved portion then soon solidified. This product melted at 29—31° and was identified as Δ^1-*cyclo*hexene-1-carboxylic acid (compare Aschan, *Annalen*, 1892, **271**, 267). It was readily soluble in dilute aqueous sodium carbonate, from which it was reprecipitated by the addition of hydrochloric acid. Its solution in chloroform, after addition of the calculated amount of bromine, was kept for 2 hours, the solvent removed by evaporation, and the residue recrystallised from benzene–petroleum, from which 1 : 2-dibromo*cyclo*hexane-1-carboxylic acid separated in colourless prisms, m. p. 144° (compare Aschan, *loc. cit.*). That portion of the distillate which dissolved in dilute hydrochloric acid was identified as aniline by conversion into acetanilide.

*ψ-Indoxyl*spirocyclo*hexane* (III).—A mixture of 1-anilino*cyclo*hexane-1-carboxylic acid (35 g.) and potassium hydroxide (90 g.) was heated to 340—350°, maintained at that temperature for ½ hour, allowed to cool, and treated with an excess of water. The insoluble portion was ground with water and dried in a desiccator over sulphuric acid. The crude product (14 g., melting indefinitely at about 80°) was distilled; the yellow, oily distillate solidified on rubbing with petroleum. After recrystallisation from petroleum, the product (m. p. 110—117°) was further purified by boiling it with acetic anhydride (50 c.c.) for an hour, cooling the solution and shaking it with an excess of water, and recrystallising the 7-*acetyl*-*ψ-indoxyl*spirocyclo*hexane* so obtained from methyl alcohol, from which it separated in large, colourless prisms (6 g.), m. p. 105° (Found: N, 5·7. $C_{15}H_{17}O_2N$ requires N, 5·7%). A solution of the acetyl derivative in alcohol (90 c.c.) and water (60 c.c.), containing

potassium hydroxide (18 g.), was boiled for ½ hour and thereafter diluted with water; *ψ-indoxyl*spirocyclo*hexane* (4 g.) then separated in a pure condition. It can be crystallised from petroleum and obtained in colourless prisms, m. p. 124° (Found: C, 77·8; H, 7·5; N, 6·8. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·4; N, 7·0%).

ψ-Indoxyl*spirocyclo*hexane is not altered, even on boiling, by dilute hydrochloric acid or dilute sodium hydroxide solution. When heated in a steel tube at 200—210° with an excess of 20% aqueous sodium hydroxide, it was converted into a *sodium* derivative, which could be removed by filtration through asbestos. The sodium derivative (Found: Na, 9·7. $C_{13}H_{14}ONNa$ requires Na, 10·3%) did not melt up to 350° and was immediately hydrolysed, on grinding with water, to give *ψ*-indoxyl*spirocyclo*hexane. On warming with dry benzene or toluene, the substance dissolved almost completely, and on filtering and cooling the solution *ψ*-indoxyl*spirocyclo*hexane separated—which seems to indicate that combined water is present in the sodium derivative.

When a solution of *ψ*-indoxyl*spirocyclo*hexane in alcohol was treated with a few drops of concentrated hydrochloric acid and a few drops of a concentrated solution of sodium nitrite, kept for 15 minutes, and then diluted with water, the substance was recovered completely unchanged. The substance was also recovered unchanged from attempts to make a semicarbazone.

When *ψ*-indoxyl*spirocyclo*hexane (3 g.) was heated with a mixture of nitric acid (30 c.c. of *d* 1·4) and water (120 c.c.), the liquid at first became green and a dark green oil separated. The colour rapidly changed to yellow and, after boiling for 3 minutes, the mixture was cooled and the solid recrystallised from dilute alcohol, from which 10-*nitro-ψ-indoxyl*spirocyclo*hexane* separated in pink prisms, m. p. 177—178° (Found: N, 11·3. $C_{13}H_{14}O_3N_2$ requires N, 11·4%). 10-Nitro-*ψ*-indoxyl*spirocyclo*hexane is soluble in very dilute aqueous sodium hydroxide to give a deep yellow solution, but from more concentrated solutions the sodium salt separates as a yellow solid, which may be dissolved by warming. When an excess of methyl sulphate was shaken with the warm solution in aqueous sodium hydroxide, a yellow product immediately separated, and, after recrystallisation from dilute alcohol, 10-*nitro*-7-*methyl-ψ-indoxyl*spirocyclo*hexane* was obtained in yellow plates, m. p. 129° (Found: N, 10·9. $C_{14}H_{16}O_3N_2$ requires N, 10·8%). No methyl iodide was obtained on heating the substance with hydriodic acid under the usual conditions of a Zeisel experiment, so it is evident that the methyl group is attached to nitrogen and is not present as methoxyl.

One of the authors (R. L. B.) wishes to thank the Imperial Order of the Daughters of the Empire (Canada) for a scholarship which enabled him to take part in the research.

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OXFORD. [*Received, April 8th*, 1927.]

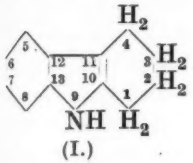
CLXXXIV.—*Substitution in Hexahydrocarbazole Derivatives.*

By JOHN GURNEY and SYDNEY GLENN PRESTON PLANT.

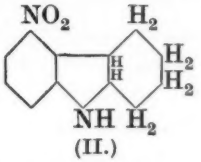
THE action of nitric acid on tetrahydrocarbazole (I) and its 9-acyl derivatives was found to give rise, among other products, to nitro-compounds which appeared at first sight to be formed by a reversal of the ordinary rules of substitution (Perkin and Plant, J., 1921, **119**, 1825; 1923, **123**, 676). The double linking in tetrahydrocarbazole has been shown to be a very active one, and the formation of these compounds can be explained, as was pointed out by Professor Robinson, by taking the view that the orienting influence is transmitted through this linking. In hexahydrocarbazole, this double bond is absent, and the introduction of substituents into this molecule ought to give results which are different from those observed with tetrahydrocarbazole. We have now investigated this problem and established the constitutions of the products with respect to those of the corresponding tetrahydrocarbazole derivatives.

The structures assigned to the nitro-compounds obtained from hexahydrocarbazole and its 9-acyl derivatives depend upon the configurations of the four isomeric mononitrotetrahydrocarbazoles. Three of these are obtained synthetically from *cyclo*hexanone-*o*-, -*m*-, and -*p*-nitrophenylhydrazone, respectively, by Fischer's indole synthesis (Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 53), whilst the fourth is prepared from 9-acetyltetrahydrocarbazole (Perkin and Plant, *loc. cit.*). There is no doubt at all about the configurations of 6-nitro- and 8-nitro-tetrahydrocarbazole. The sole product obtained when ring closure takes place by loss of ammonia from *cyclo*hexanone-*m*-nitrophenylhydrazone has been assumed by Borsche, Witte, and Bothe to be 7-nitrotetrahydrocarbazole, but it may possibly be the 5-nitro-compound, whilst the fourth isomeride, assumed in consequence by Perkin and Plant to be 5-nitrotetrahydrocarbazole, may be the 7-nitro-derivative. Ring closure in the case of the corresponding *cyclo*hexanone-*m*-carboxyphenylhydrazone does, in fact, give both of the two alternative

products (Collar and Plant, J., 1926, 808). Both the 5- and the 7-position are, however, meta with respect to the >NH group.



(I.)



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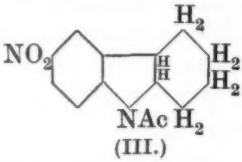

(III.)

The nitration of hexahydrocarbazole in concentrated sulphuric acid solution gives a single product, which has been identified as *5-nitrohexahydrocarbazole* (II). Its structure has been established by reducing it to the corresponding *5-aminohexahydrocarbazole*, which has also been prepared by the reduction of 5-aminotetrahydrocarbazole. The nitration of 9-methylhexahydrocarbazole under the same conditions gives a product which must be *5-nitro-9-methylhexahydrocarbazole*, since it is identical with the substance obtained by methylating 5-nitrohexahydrocarbazole. Von Braun and Ritter (*Ber.*, 1922, **55**, 3802) nitrated 9-ethylhexahydrocarbazole in concentrated sulphuric acid and obtained a compound, m. p. 142°, which they assumed, without proof, to be 7-nitro-9-ethylhexahydrocarbazole. If the structures assigned to the nitrotetrahydrocarbazoles are correct, this substance is 5-nitro-9-ethylhexahydrocarbazole, since it can also be obtained by ethylation of 5-nitrohexahydrocarbazole. In any case, the statement of von Braun and Ritter that the nitro-group takes up a position which is meta with respect to the >NH group is correct.

The action of nitric acid on 9-acetylhexahydrocarbazole in glacial acetic acid gave unexpected products. From the reaction mixture, *6-nitro-9-acetylhexahydrocarbazole* (III) was isolated. The structure of this compound was established by hydrolysing it to *6-nitrohexahydrocarbazole* and reducing the latter to the corresponding *amine*, which gave a *diacetyl* derivative on treatment with acetic anhydride. The same diacetyl derivative was obtained when 6-aminotetrahydrocarbazole was reduced electrolytically, and the product treated in the same way with acetic anhydride. In addition to 6-nitro-9-acetylhexahydrocarbazole, 5-nitro-9-acetyltetrahydrocarbazole and 9-acetyl-10 : 11-dihydroxyhexahydrocarbazole were isolated in considerable quantities from the product. The latter two substances are the compounds formed when nitric acid acts under the same conditions on 9-acetyltetrahydrocarbazole (Perkin and Plant, *loc. cit.*). It thus appears that only a portion of the 9-acetylhexahydrocarbazole undergoes nitration under these conditions, the remainder being oxidised to 9-acetyltetrahydrocarbazole, which is then acted on by more nitric acid in the way previously

established. In concentrated sulphuric acid, nitration of 9-acetylhexahydrocarbazole to the 6-nitro-derivative proceeds without any appreciable side reactions.

When nitric acid was allowed to react with 9-benzoylhexahydrocarbazole in glacial acetic acid, some oxidation to 9-benzoyltetrahydrocarbazole again first took place. The isolation of all the products of this reaction in a pure state was not achieved on account of their great solubility in acetic acid, but on using a small quantity of solvent and seeding the solution with a crystal of 11-nitro-9-benzoyl-10-hydroxyhexahydrocarbazole, there separated a considerable quantity of that substance, which is one of the two products obtained when nitric acid acts on 9-benzoyltetrahydrocarbazole (Perkin and Plant, *loc. cit.*; 9-benzoyltetrahydrocarbazole and 9-acetyltetrahydrocarbazole react in different ways with nitric acid). Direct nitration of 9-benzoylhexahydrocarbazole was accomplished in concentrated sulphuric acid, the product being *6-nitro-9-benzoylhexahydrocarbazole*, its structure being established by the fact that it gave 6-nitrohexahydrocarbazole, identical with the substance obtained from 9-acetylhexahydrocarbazole, on hydrolysis.

Bromination of hexahydrocarbazole in glacial acetic acid gave *6-bromohexahydrocarbazole*, the structure of which is established by the fact that it is identical with 6-bromohexahydrocarbazole prepared by the reduction of 6-bromotetrahydrocarbazole. The bromination of 9-acetyl- and 9-benzoyl-hexahydrocarbazole proceeded in the same way to give *6-bromo-9-acetylhexahydrocarbazole* and *6-bromo-9-benzoylhexahydrocarbazole* respectively, both of which gave 6-bromohexahydrocarbazole on hydrolysis.

It is clear from these results that substitution in hexahydrocarbazole takes quite a different course from that observed with tetrahydrocarbazole, and that the compound may be considered for this purpose as a simple benzene derivative.

Experimental.

The Nitration of Hexahydrocarbazole and 9-Methylhexahydrocarbazole.

The hexahydrocarbazole used in these experiments was prepared by the electrolytic reduction of tetrahydrocarbazole (see Perkin and Plant, J., 1924, **125**, 1512).

5-Nitrohexahydrocarbazole.—A solution of hexahydrocarbazole (30 g.) in concentrated sulphuric acid (300 c.c.) was treated gradually with powdered potassium nitrate (17·5 g.), the temperature being kept at 3°, allowed to remain for 15 minutes, and then poured on ice. The solution was kept at 0° by the addition of ice, and made alkaline with ammonia; the oily product then soon solidified (m. p. 68°).

After crystallisation from alcohol, 5-*nitrohexahydrocarbazole* was obtained in lemon-yellow needles, m. p. 69° (Found: N, 12·8. $C_{12}H_{14}O_2N_2$ requires N, 12·8%). 5-*Nitro*-9-*acetylhexahydrocarbazole* was obtained when a mixture of 5-nitrohexahydrocarbazole (5 g.) and acetic anhydride (10 g.) was kept at 110° for 3 hours, cooled, and shaken with an excess of water. It separated from alcohol in pale yellow, square plates, m. p. 142° (Found: N, 10·5. $C_{14}H_{16}O_3N_2$ requires N, 10·8%).

5-*Aminohexahydrocarbazole*.—A solution of 5-nitrohexahydrocarbazole (10 g.) in sulphuric acid (150 c.c. of 60%) was reduced for 10 hours in the cathode compartment of an electrolytic cell, lead electrodes and a current of 4·1 amps. (0·02 amp. per sq. cm. of cathode) being used, and the cell being kept in cold water. After dilution with an equal volume of water and filtering, the mixture was made alkaline with ammonia, crushed ice also being added. The solid product was crystallised from alcohol, from which 5-*aminohexahydrocarbazole* separated in colourless prisms, m. p. 111° (Found: N, 14·9. $C_{12}H_{16}N_2$ requires N, 14·9%). Yield, 55% of the theoretical.

5-Aminohexahydrocarbazole was also obtained by reducing a solution of 5-aminotetrahydrocarbazole hydrochloride (3 g., prepared as described by Edwards and Plant, J., 1923, **123**, 2395) in sulphuric acid (100 c.c. of 60%) in the electrolytic cell as before, but keeping it immersed in boiling water for 16 hours. The solution was then filtered and made alkaline at 0° with ammonia, and the product was extracted with ether. After the extract had been dried over potassium carbonate and the solvent removed, the residue solidified on rubbing, and, after recrystallisation from alcohol, 5-aminohexahydrocarbazole (0·4 g.) was obtained in colourless prisms; these, alone or mixed with the 5-aminohexahydrocarbazole described above, melted at 111°.

Both products gave the same diacetyl derivative on being heated with an excess of acetic anhydride at 100° for 15 minutes. After the solution had been cooled, and shaken with an excess of water, the solid obtained was crystallised from acetone, 5-*acetamido*-9-*acetylhexahydrocarbazole* separating in colourless prisms, m. p. 163° (Found: N, 10·1. $C_{16}H_{20}O_2N_2$ requires N, 10·3%).

5-*Nitro*-9-*methylhexahydrocarbazole*.—9-Methylhexahydrocarbazole was prepared by the reduction of 9-methyltetrahydrocarbazole (Perkin and Plant, *loc. cit.*). This substance shows a marked tendency to remain in a supercooled condition (a specimen is still completely liquid after 3 years) and has hitherto been described as a colourless oil (see also von Braun and Ritter, *loc. cit.*), but it can be crystallised from alcohol, from which it separates in colourless prisms,

m. p. 50° (Found : N, 7·4. Calc. : N, 7·5%). A solution of 9-methylhexahydrocarbazole (1 g.) in concentrated sulphuric acid (30 c.c.) was treated below 3° with potassium nitrate (0·55 g.), allowed to remain for 5 minutes, poured on ice, made alkaline with ammonia, and saturated with sodium chloride. The solid produced (m. p. 49—50°) was crystallised from alcohol, from which 5-*nitro*-9-*methylhexahydrocarbazole* (0·6 g.) separated in bright yellow needles, m. p. 52° (Found : N, 12·2. $C_{13}H_{16}O_2N_2$ requires N, 12·1%).

5-Nitro-9-methylhexahydrocarbazole was also prepared by heating 5-nitrohexahydrocarbazole (1 g.) with methyl iodide (3·5 g.) in a sealed tube at 100° for 2 hours, removing the excess of methyl iodide, treating the residue with dilute aqueous sodium hydroxide and extracting the solution with ether. After the ether had been removed, the residue was recrystallised from alcohol, from which the product separated in yellow needles; these, alone or mixed with the 5-nitro-9-methylhexahydrocarbazole described above, melted at 50°.

5-*Nitro*-9-*ethylhexahydrocarbazole*.—5-Nitrohexahydrocarbazole was ethylated by a process similar to that described for the methylation, but the reaction was much slower and heating was continued for 18 hours. The product was recrystallised from alcohol, from which 5-nitro-9-ethylhexahydrocarbazole separated in bright yellow prisms, m. p. 143° (Found : N, 11·5. Calc. : N, 11·4%). This product is evidently identical with that described by von Braun and Ritter (*loc. cit.*).

Action of Nitric Acid on 9-*Acetylhexahydrocarbazole.*

A solution of 9-acetylhexahydrocarbazole (50 g., prepared by the direct acetylation of hexahydrocarbazole; Graebe and Adlerskron, *Annalen*, 1880, **202**, 25) in glacial acetic acid (50 c.c.) was treated gradually at 23—25° with a mixture of nitric acid (26·5 g. of *d* 1·4) and glacial acetic acid (75 c.c.). After 2 hours, the mixture was poured into water; the product then gradually solidified to a yellow mass, from which three substances were isolated in a pure condition. After repeated crystallisation from acetone, a small quantity (0·2 g.) of glistening, colourless plates, m. p. 204°, was obtained. An analysis (Found : N, 6·0. Calc. : N, 5·7%) and a mixed m.-p. determination showed that this substance was 9-acetyl-10 : 11-dihydroxyhexahydrocarbazole, one of the products obtained when nitric acid acts on 9-acetyltetrahydrocarbazole in glacial acetic acid. The mixture in the acetone mother-liquor, on repeated crystallisation from glacial acetic acid, yielded yellow needles (5 g.), m. p. 175°, which an analysis (Found : N, 10·8. Calc. : N, 10·9%) and

a mixed m.-p. determination proved to be 5-nitro-9-acetyltetrahydrocarbazole, the other of the two products from 9-acetyltetrahydrocarbazole. Further proof of the structure of this compound was obtained on boiling it for a short time with aqueous-alcoholic sodium hydroxide, diluting the solution with water, and recrystallising the product from alcohol, from which 5-nitrotetrahydrocarbazole separated in yellow prisms, m. p. 172°. From the acetone and glacial acetic acid mother-liquors there was isolated by repeated fractional crystallisation a product which ultimately separated from acetone in lemon-yellow prisms (5 g.), m. p. 150°, and was shown to be 6-*nitro*-9-*acetylhexahydrocarbazole* (Found : N, 10·7. $C_{14}H_{16}O_3N_2$ requires N, 10·8%). The solution of this product (1 g.) in a mixture of alcohol (15 c.c.) and aqueous sodium hydroxide (15 c.c. of 30%) was boiled for 20 minutes and then poured into water. After crystallisation from alcohol, 6-*nitrohexahydrocarbazole* was obtained in bright yellow prisms, m. p. 84° (Found : N, 12·6. $C_{12}H_{14}O_2N_2$ requires N, 12·8%).

6-Nitro-9-acetylhexahydrocarbazole is more easily obtained by nitration in concentrated sulphuric acid solution. 9-Acetylhexahydrocarbazole (5 g.), dissolved in sulphuric acid (40 c.c.), was treated with potassium nitrate (2·3 g.) at 5—7°, the solution poured, after a short time, on ice, and the product crystallised from acetone, from which 6-nitro-9-acetylhexahydrocarbazole separated in yellow prisms, m. p. 150°. The m. p. of the mixture with the 6-nitro-9-acetylhexahydrocarbazole described above showed no depression. The hydrolysis of this product was also carried out by heating it for an hour on the steam-bath with concentrated hydrochloric acid, and, on cooling, the *hydrochloride* of 6-nitrohexahydrocarbazole separated. After recrystallisation from alcohol, it was obtained in pale yellow plates, m. p. 199° (Found : N, 11·2. $C_{12}H_{15}O_2N_2Cl$ requires N, 11·0%). This hydrochloride readily yielded 6-nitrohexahydrocarbazole, m. p. 84°, on treatment with dilute aqueous sodium hydroxide.

6-*Aminohexahydrocarbazole*.—A solution of 6-nitrohexahydrocarbazole (5 g.) in sulphuric acid (140 c.c. of 60%) was reduced electrolytically for 15 hours by the method described above, the cell being kept immersed in cold water. After the solution had been diluted with an equal volume of water, filtered, and made alkaline at 0° with concentrated ammonia, the mixture was extracted with ether, and the ethereal solution dried over potassium carbonate. The viscous, oily 6-*aminohexahydrocarbazole* remaining after removal of the ether could not readily be made to crystallise, so it was treated with an excess of acetic anhydride at room temperature. The

product separated on rubbing, and, after the whole had been shaken with an excess of water and then crystallised from alcohol, 6-*acetamido*-9-*acetylhexahydrocarbazole* was obtained in colourless needles (1·2 g.), m. p. 213° (Found: N, 10·3. $C_{16}H_{20}O_2N_2$ requires N, 10·3%).

6-Aminohexahydrocarbazole was also obtained by the electrolytic reduction of a solution of 6-aminotetrahydrocarbazole (4 g., prepared as described by Edwards and Plant, *loc. cit.*) in sulphuric acid (120 c.c. of 60%), a current of 5 amps. being used for 22 hours at room temperature. After the solution had been diluted with water (60 c.c.), filtered, and made alkaline with concentrated ammonia at 0°, a colourless solid separated. This (0·5 g.), after crystallisation from toluene, proved to be unchanged 6-aminotetrahydrocarbazole. The aqueous solution was extracted with ether, and from the ethereal solution the oily 6-aminohexahydrocarbazole was obtained as before. On treatment with acetic anhydride as described above, 6-acetamido-9-acetylhexahydrocarbazole (0·5 g.), m. p. 212°, was formed. A mixture of the two products, prepared by different methods, also melted at 212°.

7-*Acetamido*-9-*acetylhexahydrocarbazole*.—This derivative was prepared during the course of the present work, although it has not been required in order to establish the structure of any compound obtained directly from hexahydrocarbazole. A solution of 7-aminotetrahydrocarbazole hydrochloride (4 g., prepared as described by Edwards and Plant, *loc. cit.*) in sulphuric acid (140 c.c. of 60%) was reduced electrolytically by a current of 5 amps. for 36 hours at 100°; it was then diluted with water, made alkaline with ammonia, and shaken with ether. After being dried with potassium carbonate, the ether was removed and 7-*aminohexahydrocarbazole* remained as a brown oil; this was warmed with an excess of acetic anhydride at 100° for a minute and shaken with an excess of water, and the product was crystallised from alcohol, 7-*acetamido*-9-*acetylhexahydrocarbazole* being obtained in colourless prisms, m. p. 233° (Found: N, 10·4. $C_{16}H_{20}O_2N_2$ requires N, 10·3%).

Action of Nitric Acid on 9-*Benzoylhexahydrocarbazole*.

9-Benzoylhexahydrocarbazole was prepared by shaking a suspension of hexahydrocarbazole in an excess of a 10% aqueous solution of potassium hydroxide with benzoyl chloride (1¼ mols.). The product separated from alcohol in colourless needles, m. p. 106° (compare von Braun, *Ber.*, 1910, **43**, 2880, who describes it as an oil, b. p. 270°/10 mm.) (Found: N, 4·9. Calc.: N, 5·1%). A solution of 9-benzoylhexahydrocarbazole (5 g.) in glacial acetic

acid (15 c.c.) was treated at 60—67° with a mixture of nitric acid (1·9 g. of *d* 1·4) and glacial acetic acid (1 c.c.). The product was cooled, a crystal of 11-nitro-9-benzoyl-10-hydroxyhexahydrocarbazole (prepared from 9-benzoyltetrahydrocarbazole) added, and the whole stirred for 3 hours. The colourless prisms (0·1 g.), m. p. 146°, that separated were shown by a mixed m.-p. determination to be 11-nitro-9-benzoyl-10-hydroxyhexahydrocarbazole. When the acetic acid mother-liquor was poured into water, a thick, pale yellow oil separated, but attempts to obtain crystalline substances from this were unsuccessful.

6-*Nitro*-9-*benzoylhexahydrocarbazole*.—A solution of 9-benzoylhexahydrocarbazole (25 g.) in concentrated sulphuric acid (200 c.c., was treated gradually at 10—12° with potassium nitrate (9·1 g.), kept for 30 minutes, and then poured on ice. The yellow solid which separated was recrystallised from alcohol, from which 6-*nitro*-9-*benzoylhexahydrocarbazole* separated slowly in clusters of yellow prisms, m. p. 106—107° (Found: N, 8·7. $C_{19}H_{18}O_3N_2$ requires N, 8·7%). When a solution of this nitro-compound (6 g.) in a mixture of alcohol (100 c.c.) and aqueous sodium hydroxide (75 c.c. of 30%) was boiled for 20 minutes and then poured into cold water, 6-nitrohexahydrocarbazole, which separated from alcohol in yellow prisms, m. p. 84°, was precipitated. The m. p. of a mixture of this product and 6-nitrohexahydrocarbazole obtained from the corresponding acetyl derivative showed no depression.

Bromination of Hexahydrocarbazole Derivatives.

6-*Bromohexahydrocarbazole*.—A solution of hexahydrocarbazole (5 g.) in glacial acetic acid (50 c.c.) was treated gradually at room temperature with bromine (1·8 c.c.). An oily product separated, and, after the addition of all the bromine, the mixture was heated for a minute on the steam-bath; a clear solution was then obtained. On cooling, colourless crystals of the *hydrobromide* (6·3 g.), m. p. 203° (decomp.), separated, and this product, when treated with dilute aqueous sodium hydroxide, yielded 6-*bromohexahydrocarbazole*, which separated from alcohol in colourless, pentagonal plates, m. p. 75° (Found: N, 5·8. $C_{12}H_{14}NBr$ requires N, 5·6%).

The preparation of 6-bromohexahydrocarbazole by the electrolytic reduction of 6-bromotetrahydrocarbazole (prepared as described by Borsche, Witte, and Bothe, *loc. cit.*) had previously been carried out by Miss E. I. Postgate. A suspension of 6-bromotetrahydrocarbazole (4 g.) in sulphuric acid (100 c.c. of 60%) was reduced by a current of 5 amps. (0·02 amp. per sq. cm. of cathode) during 7 hours,

the cell being immersed in boiling water. After being diluted to 200 c.c. and filtered from any unchanged 6-bromotetrahydrocarbazole, the solution was made alkaline at 0° with concentrated ammonia; the 6-bromohexahydrocarbazole which separated was crystallised from alcohol and obtained in colourless, pentagonal plates, m. p. 75°. The mixture of these two specimens of 6-bromohexahydrocarbazole also melted at 75°.

6-*Bromo*-9-*acetylhexahydrocarbazole*.—A solution of 9-acetylhexahydrocarbazole (15 g.) in glacial acetic acid (24 c.c.) was treated gradually with bromine (3·6 c.c.), the mixture being kept cool in ice-water. When the reaction had finished, the yellow oil which had separated was dissolved by warming the mixture to 60°, and, on cooling and rubbing, a bright yellow, crystalline product, m. p. 132—134° (decomp.), was obtained. This appeared to be a *hydrobromide* of 6-bromo-9-acetylhexahydrocarbazole, since, on warming it with water or, more readily, by treating it with dilute aqueous potassium hydroxide and then recrystallising the product from alcohol, 6-*bromo*-9-*acetylhexahydrocarbazole* was obtained in long, colourless prisms, m. p. 104° (Found: N, 4·8. $C_{14}H_{16}ONBr$ requires N, 4·8%). After a solution of 6-bromo-9-acetylhexahydrocarbazole in aqueous-alcoholic sodium hydroxide had been boiled for 8 hours, it was poured into water, and the product recrystallised from alcohol; 6-bromohexahydrocarbazole, identical in every way with the specimens described above, separated.

6-*Bromo*-9-*benzoylhexahydrocarbazole*.—A solution of 9-benzoylhexahydrocarbazole (5 g.) in glacial acetic acid (20 c.c.) was treated gradually at room temperature with bromine (1 c.c.), then warmed to 60°, diluted with water, and made alkaline with ammonia. The oily product solidified on standing, and, after crystallisation from alcohol, 6-*bromo*-9-*benzoylhexahydrocarbazole* was obtained in colourless needles (4·2 g.), m. p. 125° (Found: N, 3·8. $C_{19}H_{18}ONBr$ requires N, 3·9%). This product was hydrolysed by boiling it with aqueous-alcoholic potassium hydroxide for 10 hours; the mixture was poured into water, and on recrystallising the precipitate from alcohol, 6-bromohexahydrocarbazole, identical with the specimens described above, was obtained.

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CLXXXV.—*The Action of Halogen-substituted Phenylhydrazines upon Dihydroxytartaric Acid.*

By FREDERICK DANIEL CHATTAWAY and WILLIAM GERALD HUMPHREY.

THE action of hydrazines upon dihydroxytartaric acid was first studied by Ziegler and Locher (*Ber.*, 1887, **20**, 834), but many of their conclusions were later shown to be incorrect. Repetition of their work by Knorr (*Ber.*, 1888, **21**, 1201), Anschutz (*Annalen*, 1896, **294**, 219), and Gnehm and Benda (*Annalen*, 1897, **299**, 100) showed that the nature of the product depends upon the substituents in the nucleus; thus ordinary phenylhydrazine gives the expected osazone, while phenylhydrazine-*p*-sulphonic acid gives a pyrazolone derivative (tartrazine). The unsubstituted osazone may be converted into a pyrazolone derivative corresponding to tartrazine by crystallisation from acetic acid. Gnehm and Benda (*loc. cit.*) made the further important observation that, when this osazone is crystallised from acetic anhydride, water is lost in a second manner giving an acid anhydride isomeric with the pyrazolone derivative.

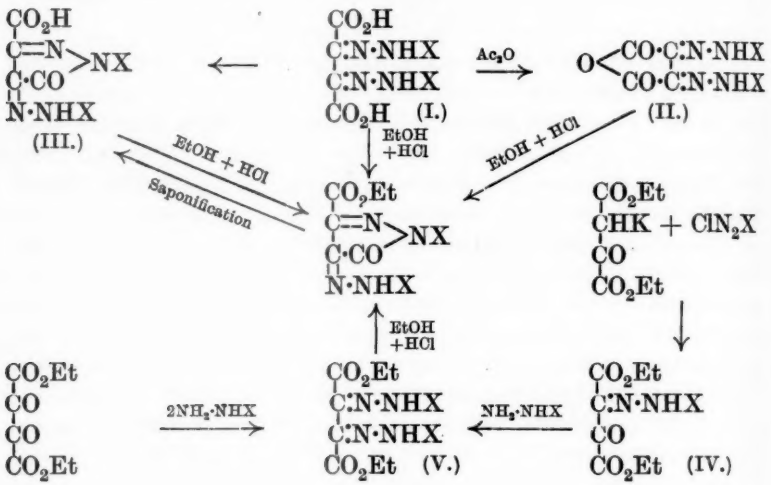
In the present paper, the influence of halogen substituents in the phenyl residues upon the ease of formation from the osazones of the pyrazolone and anhydride ring systems is described. The compounds thus obtained are similar in properties to the corresponding unsubstituted compounds, the accumulation of halogen in the phenyl groups being attended only by a diminishing solubility and a greater tendency towards formation of the anhydride in preference to the pyrazolone.

The osazones are sparingly soluble substances which cannot be crystallised unchanged from any solvent. On heating with acetic anhydride or benzoyl chloride, they are converted into deep red anhydrides. These anhydrides are unaffected by prolonged boiling with water, but dissolve in warm aqueous sodium carbonate to give solutions of the disodium salts of the osazones. On heating with alcohols containing hydrogen chloride, esters of the isomeric pyrazolone acids are formed.

The osazones are converted into hydrazones of diketopyrazolinecarboxylic acids by crystallisation from acetic acid or by acidification of their sodium salts. In the former reaction, varying amounts of the isomeric anhydrides are simultaneously produced. These pyrazoline derivatives are sparingly soluble, yellow or orange-yellow solids which undergo esterification only with difficulty. Their esters are more easily obtained from the corresponding osazone or anhydride.

The structure of the pyrazolone derived from the 2 : 4-dibromophenylosazone has been confirmed by two syntheses.

The following scheme represents the reactions with 2 : 4-dibromophenylhydrazine, X denoting $C_6H_3Br_2$:



EXPERIMENTAL.

Preparation of Sodium Dihydroxytartrate.—Finely powdered tartaric acid (200 g.) is suspended in 280 c.c. of nitric acid (*d* 1·42) and 500 c.c. of concentrated sulphuric acid are added slowly with constant stirring. The temperature rises to about 70° and a clear solution is obtained which is covered over and allowed to cool slowly for 8—12 hours. The semi-solid pulp of tartaric acid dinitrate thus obtained is broken up, and freed from acid as completely as possible by suction and pressure; during this operation the mass should be protected from atmospheric moisture. The hard-pressed, solid mass is stirred with crushed ice until it dissolves, ice-water being added if necessary. The liquid is nearly neutralised with sodium carbonate and, after addition of a litre of saturated sodium acetate solution, filtered and left in a cool place for 2—3 days; at first colourless, it becomes green, owing to the liberation of oxides of nitrogen, and finally colourless when these have escaped. Sodium dihydroxytartrate separates as a very sparingly soluble, white powder, which is filtered off, washed with cold water, and dried by exposure to air.

Preparation of Halogen-substituted Phenylhydrazines.—The reduction of the diazonium salts with stannous chloride, the method previously described for the preparation of the mono- and di-halogen-

substituted phenylhydrazines, is not altogether satisfactory on a large scale on account of the cost of the materials and the difficulty of completely removing the tin from the products. The following modification of Fischer's method of reduction with sodium sulphite gives much better results.

A suspension of the finely powdered amine ($\frac{1}{5}$ g.-mol.) in 70 c.c. of concentrated hydrochloric acid (excess) is warmed to about 60° for 1 hour to convert the amine into its hydrochloride, and is then cooled in a freezing mixture, and an ice-cold solution of sodium nitrite (20 g. in 50 c.c. of water) is added, with vigorous stirring, during not less than 1 hour. The diazonium solution is filtered and added slowly to a solution of sodium sulphite, prepared by passing sulphur dioxide into a solution of 45 g. of sodium hydroxide in 300 c.c. of water until an acid reaction is just indicated by phenolphthalein. (An excess of sulphur dioxide must be avoided; otherwise tarry matters are produced on addition of the diazonium solution and the yield of hydrazine is greatly diminished.) The resulting bright orange solution is warmed to 60°, and made acid to litmus by the addition of concentrated hydrochloric acid (about 20 c.c.); the colour then changes to pale yellow. The solution is heated for about an hour, 100 c.c. of concentrated hydrochloric acid are added, and the mixture is allowed to cool. The hydrazine hydrochloride crystallises as a pulp of small needles, which are filtered off and recrystallised from dilute hydrochloric acid (1 : 4). The yield of the air-dried product is 80—90% of the theoretical.

Diketosuccinic acid 2 : 4-*dibromophenylosazone* (I) was prepared by adding a solution of 26 g. of sodium dihydroxytartrate (1 mol.) in 180 c.c. of moderately concentrated hydrochloric acid (1 : 1) to a fine suspension of 60 g. of 2 : 4-dibromophenylhydrazine hydrochloride (2 mols.) in 1500 c.c. of very dilute hydrochloric acid (1 : 100). The mixture was stirred for 6 hours and afterwards heated at 80° for 2 hours. The *osazone*, which separated as a soft, orange-coloured powder, was filtered off without previous cooling, repeatedly washed with boiling water, and dried at 110°. It was thus obtained as an orange powder, m. p. 205° (decomp.) (Found: Br, 50·1. $C_{16}H_{10}O_4N_4Br_4$ requires Br 49·8%).

Anhydrodiketosuccinic Acid 2 : 4-*Dibromophenylosazone* (II).—The osazone (I) was added to boiling acetic anhydride until no more would dissolve. A clear, deep red solution was thus obtained which on cooling deposited the *anhydride* in large, red, elongated prisms, m. p. 267° (decomp.) (Found: Br, 51·35. $C_{16}H_8O_3N_4Br_4$ requires Br, 51·3%).

1-2′ : 4′-*Dibromophenyl*-4 : 5-*diketopyrazoline*-3-*carboxylic acid* 4-2″ : 4″-*dibromophenylhydrazone* (III) is formed together with the

isomeric anhydride (II) on crystallising the osazone (I) from acetic acid. The two isomerides are readily distinguished owing to their marked difference in colour and crystalline form. Their separation by crystallisation from acetic acid, although difficult on account of their sparing solubility, can be effected as follows: A saturated, boiling solution, during cooling to 70°, deposits most of (III) together with some of the anhydride; below this temperature, the anhydride continues to separate with only a small amount of the pyrazolone. By repeating the process with each of the two fractions the substances are obtained pure.

The compound (III) is, however, best obtained by acidifying the deep brown solution produced by boiling its ethyl ester (see below) (5 g.) for 4 hours with 200 c.c. of 10% sodium hydroxide solution; the orange-yellow powder thus obtained separates from acetic acid in clusters of minute, orange-yellow crystals, m. p. 248° (decomp.) (Found: Br, 51·4. $C_{16}H_8O_3N_4Br_4$ requires Br, 51·3%).

The *methyl* ester of the acid (III) is best obtained by heating the anhydride (II) in a sealed tube with methyl alcohol, containing 2% of dry hydrogen chloride, for 8 hours at 100°. It is moderately easily soluble in acetic acid, from which it separates in very small, orange-yellow needles, m. p. 233° (Found: Br, 50·2. $C_{17}H_{10}O_3N_4Br_4$ requires Br, 50·2%). The *ethyl* ester, obtained by boiling the osazone (I), the anhydride (II), or the pyrazolone (III) with alcohol containing 5% of dry hydrogen chloride, crystallises from acetic acid, in which it is moderately easily soluble, in long, slender, yellow prisms, m. p. 229° (Found: Br, 49·0. $C_{18}H_{12}O_3N_4Br_4$ requires Br, 49·1%). The n-*butyl* ester, which is similarly prepared, is easily soluble in acetic acid, from which it separates in yellow, glistening plates, m. p. 175° (Found: Br, 47·0. $C_{20}H_{16}O_3N_4Br_4$ requires Br, 47·1%).

Ethyl diketosuccinate 2 : 4-*dibromophenylhydrazone* (IV) is not readily obtained pure from ethyl diketosuccinate owing to the simultaneous formation of the osazone. It is, however, readily prepared from ethyl oxalacetate. A cold aqueous solution of 2 : 4-dibromobenzenediazonium chloride is added slowly and with vigorous stirring to an aqueous solution of the potassium derivative of ethyl oxalacetate, cooled in a freezing mixture. A sticky red mass separates from which, by repeated crystallisation from alcohol, the *hydrazone* is obtained in small, pale yellow, compact prisms, m. p. 95° (Found: Br, 35·4. $C_{14}H_{14}O_5N_2Br_2$ requires Br, 35·55%).

Ethyl diketosuccinate 2 : 4-*dibromophenylosazone* (V) cannot be prepared by the direct esterification of the osazone (I) on account of simultaneous pyrazolone formation. It is obtained by the action in alcoholic solution (1) of dibromophenylhydrazine upon the mono-

hydrazone, (2) of excess of dibromophenylhydrazine upon ethyl diketosuccinate. It separates from alcohol in glistening, yellow, four-sided plates, m. p. 197° (Found: Br, 45·9. $C_{20}H_{18}O_4N_4Br_4$ requires Br, 45·8%). On boiling with alcohol containing hydrogen chloride, it is converted into the ethyl ester of (III), m. p. 229°, described above.

Diketosuccinic acid p-*bromophenylosazone* (I; X = C_6H_4Br) was obtained as a soft, orange-red powder, m. p. 201° (decomp.) (Found: Br, 33·2. $C_{16}H_{12}O_4N_4Br_2$ requires Br, 33·1%).

The *anhydride* (formula as II) forms deep red, compact prisms, m. p. 262° (decomp.) (Found: Br, 34·4. $C_{16}H_{10}O_3N_4Br_2$ requires Br, 34·3%). This and all the following compounds, unless otherwise stated, are moderately easily soluble in acetic acid, from which they were crystallised.

1-p-*Bromophenyl*-4 : 5-*diketopyrazoline*-3-*carboxylic acid* 4-p-*bromophenylhydrazone* (formula as III) is sparingly soluble in acetic acid, from which it separates in very small, compact, yellow prisms, m. p. 260° (decomp.) (Found: Br, 34·5. $C_{16}H_{10}O_3N_4Br_2$ requires Br, 34·3%).

Its *methyl* ester, which is best obtained by heating the osazone anhydride in a sealed tube with methyl alcohol, containing 2% of dry hydrogen chloride, for 8 hours at 100°, forms long, thin, orange prisms, m. p. 213° (Found: Br, 33·5. $C_{17}H_{12}O_3N_4Br_2$ requires Br, 33·3%). The *ethyl* ester forms thin, orange-yellow prisms, m. p. 191° (Found: Br, 32·5. $C_{18}H_{14}O_3N_4Br_2$ requires Br, 32·4%).

Diketosuccinic acid 2 : 4-*dichlorophenylosazone* (I; X = $C_6H_3Cl_2$) was obtained as a soft, orange-red powder, m. p. 198° (decomp.) (Found: Cl, 30·9. $C_{16}H_{10}O_4N_4Cl_4$ requires Cl, 30·6%).

The *anhydride* (formula as II) forms small, elongated, red prisms, m. p. 242° (decomp.) (Found: Cl, 31·9. $C_{16}H_8O_3N_4Cl_4$ requires Cl, 31·8%).

1-2′ : 4′-*Dichlorophenyl*-4 : 5-*diketopyrazoline*-3-*carboxylic acid* 4-2″ : 4″-*dichlorophenylhydrazone* (formula as III) is sparingly soluble in acetic acid, from which it separates in nodular aggregates of very small, yellow needles, m. p. 252° (decomp.) (Found: Cl, 31·7. $C_{16}H_8O_3N_4Cl_4$ requires Cl, 31·8%).

Its *ethyl* ester forms long, fine needles, m. p. 212° (Found: Cl, 29·9. $C_{18}H_{12}O_3N_4Cl_4$ requires Cl, 29·95%).

Diketosuccinic acid p-*chlorophenylosazone* (I; X = C_6H_4Cl) was obtained as a soft, orange-red powder, m. p. 195° (decomp.) (Found: Cl, 17·7. $C_{16}H_{12}O_4N_4Cl_2$ requires Cl, 18·0%).

The *anhydride* (formula as II) forms small, slender, red prisms, m. p. 257° (decomp.) (Found: Cl, 18·9. $C_{16}H_{10}O_3N_4Cl_2$ requires Cl, 18·8%).

1-p-*Chlorophenyl*-4 : 5-*diketopyrazoline*-3-*carboxylic acid* 4-p-*chlorophenylhydrazone* (formula as III) is obtained by crystallising the osazone from acetic acid. It is rather sparingly soluble in acetic acid, from which it separates in small, orange-yellow, compact prisms, m. p. 254° (decomp.) (Found: Cl, 18·8. $C_{16}H_{10}O_3N_4Cl_2$ requires Cl, 18·8%).

Its *ethyl* ester forms very slender, orange-yellow prisms, m. p. 190° (Found: Cl, 17·7. $C_{18}H_{14}O_3N_4Cl_2$ requires Cl, 17·5%).

THE QUEEN'S COLLEGE, OXFORD. [*Received, March 30th*, 1927.]

CLXXXVI.—*The Solubility of Potassium Ferrocyanide in Water at Temperatures up to 25°.*

By REECE HENRY VALLANCE.

MANY investigators have attempted to determine the solubility of potassium ferrocyanide in water at various temperatures, but the results obtained, especially at lower temperatures, do not harmonise (see Vallance, *Chem. News*, 1922, **125**, 7). In the earlier investigations this may have been due in part to a variation in the purity or hydration of the ferrocyanide employed, or to inaccuracy in manipulation; but in recent work it appears more probable that the fault lies in the methods of estimating the amount of salt in the solution. It was deemed necessary at the outset to check the accuracy of the methods in general use, which are: (*a*) titration with potassium permanganate, (*b*) titration with a standard solution of a metallic salt, *e.g.*, of zinc or copper, and (*c*) decomposition of the ferrocyanide into hydrogen cyanide, absorption of the latter by potash, and titration with standard silver nitrate solution.

The first method has been most generally used in solubility determinations, although its accuracy has long been questioned. It does not give good results, since the colour due to a slight excess of the oxidising agent is not easily perceived, and none of the many modifications hitherto proposed was found to be entirely satisfactory.

The second method was not considered suitable for the work in view, since all estimations must be made under exactly similar conditions, and this would be difficult with a series of solutions of different concentrations, of which only limited quantities were available.

The method by which the ferrocyanide is decomposed with evolution of hydrogen cyanide has been used with fairly satisfactory results (Feld, *Chem. Zentr.*, 1903, ii, 1398; Colman, *Analyst*, 1908,

33, 261; 1910, **35**, 295), although it is found difficult to avoid loss of the acid (Skirrow, *J. Soc. Chem. Ind.*, 1910, **29**, 319; Williams, *ibid.*, 1912, **31**, 468). Williams showed that solutions of potassium ferrocyanide are catalytically decomposed when boiled with cuprous chloride in the presence of hydrochloric acid. By collecting the evolved acid in alkali, and afterwards titrating with standard silver nitrate, the ferrocyanide originally present may be estimated. This method appeared suitable for the work in view, and was therefore investigated. (The salt used throughout this research was the A.R. trihydrated potassium ferrocyanide, supplied by the British Drug Houses, Ltd.) Great care was taken to avoid loss of hydrogen cyanide, but a series of estimations gave results which were discordant to the extent of 7%, mostly low. In spite of the addition of potassium iodide, the end-point was determined only with difficulty, possibly because of the strong alkali present. Moreover, the method was inconvenient.

Attention was next directed to the method based on the decomposition of complex cyanides by persulphates in presence of mineral acids (Dittrich and Hassel, *Ber.*, 1903, **36**, 1929), 50% of the hydrogen cyanide being evolved and ammonium salts formed. The iron can then be precipitated by ammonia and estimated in the usual way. This method at first appeared satisfactory, but when it was applied to larger quantities (1—4 g.) of the ferrocyanide, the blue precipitate which formed when the acidified mixture of ferrocyanide and ammonium persulphate was heated could not be redissolved, even by the addition of hydrochloric acid and prolonged heating with excess of the persulphate. This method was used for solubility determinations by Harkins and Pearce (*J. Amer. Chem. Soc.*, 1916, **38**, 2714), who admitted that, in spite of the fact that pure hydrogen was passed through the solutions to prevent oxidation, the formation of the blue precipitate sometimes either prevented or vitiated the analyses.

It was found to be impracticable to dry and weigh the ferrocyanide in the anhydrous condition: the loss of water, after heating for definite periods at 105—110°, was always lower than that required by the trihydrate formula, unless the partial decomposition, which was nearly always apparent, became very marked. It is probable, therefore, that the true loss of water would be still lower.

It was thought that it would be more satisfactory if the iron could be converted into the ferric condition, as was attempted in the persulphate method, and many experiments were made in which the salt was heated alternately with concentrated sulphuric acid and concentrated nitric acid. After such treatment, the residue on ignition did not yield a product of constant composition (*e.g.*,

$4K_2SO_4,Fe_2O_3$) and the silica crucibles used were badly attacked. The following method, however, gave excellent results and was used throughout for the solubility determinations.

The Estimation of Iron in Potassium Ferrocyanide.

A weighed quantity of potassium ferrocyanide in a platinum dish was just covered with concentrated sulphuric acid and heated (in a fume-chamber) very gently on a sand-bath until all action had ceased, and then strongly for about ½ hour. After cooling, a little more concentrated sulphuric acid and a few drops of concentrated nitric acid were added, and the heating was repeated, at first gently and then strongly until the residue was dry; this was then cooled, gently warmed with concentrated hydrochloric acid, transferred to a 500 c.c. beaker containing a little hot water, and diluted to about 300 c.c. with water; a few drops of concentrated nitric acid were added, and the mixture was gently boiled until a clear solution was obtained; this was allowed to cool, and made up to 500 c.c. in a flask which had been graduated against a 100 c.c. pipette.

For each estimation, 100 c.c. of the solution were withdrawn by means of this pipette, and the ferric hydroxide was precipitated from the hot solution by addition of ammonium hydroxide. The precipitate was washed several times by decantation, transferred to two filters (in order to facilitate washing), thoroughly washed with hot water until the filtrate was quite free from sulphate and chloride, dried at 110°, ignited, and weighed [Found, for different specimens: Fe, (i) 13·416, (ii) 13·397, (iii) 13·403. Calc. for $K_4Fe(CN)_6,3H_2O$: Fe, 13·22%].

The results, although concordant, were higher than the value required by theory, and to a greater extent than can be accounted for by the low results obtained (p. 1329) for the loss of water on heating.

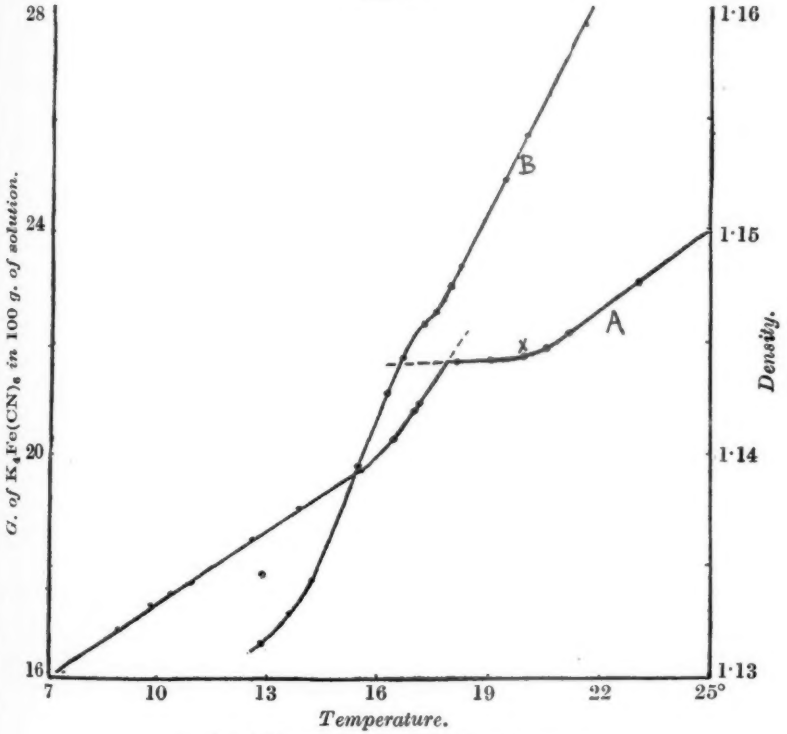
The method outlined above has also been employed by Friend and Merriman in this laboratory for the estimation of alkali ferricyanides, accurate results being obtained.

Determination of the Solubility of Potassium Ferrocyanide at Temperatures up to 25°.

The method employed was similar to that described by Lumsden (J., 1902, **81**, 350). The solution to be tested was constantly stirred in contact with the salt for about 7 hours, a portion then being drawn by suction from the saturation vessel, through a Gooch filter containing glass wool (previously washed and dried), into a receiving flask. The whole apparatus was sufficiently immersed in a thermostat for the solution to remain under water during the

transference, a constant temperature being carefully maintained. A suitable quantity of the filtered solution was immediately weighed into a platinum dish, evaporated to dryness, and the residue decomposed by means of sulphuric acid and estimated by the method already described. The results are in Table I, where s represents g. of anhydrous salt in 100 g. of saturated solution. When these results are plotted as in Fig. 1, it is seen that the solubility curve is not continuous, but that a break occurs between 17° and 18°.

FIG. 1.



A. *Solubility curve.* B. *Density curve.*

[x *Value obtained by Briggs* (loc. cit.) *for "a" salt.*]

TABLE I.

Temp.	s.	Temp.	s.	Temp.	s.	Temp.	s.
7·4°	16·043	12·6°	18·514	17·0°	20·922	* 23·1°	23·074
8·9	16·844	* 13·8	19·067	17·9	21·687	* 25·0	23·971
9·8	17·309	15·5	19·715	19·0	21·725		
* 10·4	17·541	16·3	20·240	* 20·4	21·953		
11·1	17·784	* 16·9	20·862	21·1	22·244		

* Vallance, *loc. cit.*

This points to a change in the solid phase, possibly due to a change in the degree of hydration, but it is of particular interest in view of the long-admitted possibility of the existence of two stereoisomeric forms of potassium ferrocyanide (Briggs, J., 1911, **99**, 1019; 1920, **117**, 1026; Bennett, J., 1917, **111**, 490).

The density of the saturated solution at different temperatures was next examined. A silica pyknometer of about 20 c.c. capacity was employed, and the slight change in capacity with rise in temperature was determined by weighing it full of mercury at two different temperatures. In order to fill the pyknometer with the saturated solution, it was attached to the receiving flask of the solubility apparatus whilst immersed in the thermostat, and the solution was drawn over by suction. The density was calculated from the formula

$$D^{t^\circ}_{4^\circ} = W(1—0{\cdot}0012/d)/C + 0{\cdot}0012,$$

where W = apparent weight of solution in air at t°, C = capacity of pyknometer at t°, d = density of water at t°, and 0·0012 = mean density of air.

The results are in Table II.

TABLE II.

Temp.	$D^{t^\circ}_{4^\circ}$.	Temp.	$D^{t^\circ}_{4^\circ}$.	Temp.	$D^{t^\circ}_{4^\circ}$.	Temp.	$D^{t^\circ}_{4^\circ}$.
12·8°	1·13153	16·2°	1·14295	17·9°	1·14789	21·5°	1·15811
13·7	1·13307	16·6	1·14441	18·2	1·14861	25·1	1·17041
14·2	1·13430	17·2	1·14596	19·5	1·15279		
15·4	1·13953	17·5	1·14641	20·0	1·15435		

Very few determinations have been made by previous workers, but those of Michel and Krafft (*Ann. Chim. Phys.*, 1854, **41**, 478), who give $D^{15^\circ} = 1{\cdot}1441$, of Sonstadt (J., 1906, **89**, 343), $D^{8{\cdot}9^\circ} = 1{\cdot}1191$, and of Farrow (J., 1926, 49), $D^{24{\cdot}9^\circ} = 1{\cdot}1731$, are in general agreement with the above figures. The value obtained by Harkins and Pearce (*J. Amer. Chem. Soc.*, 1916, **38**, 2714), $D^{25^\circ} = 1{\cdot}09081$, is obviously incorrect. When the results are plotted as in Fig. 1, a slight change in the direction of the curve is observable above 17°.

In order, if possible, to detect an actual transition point, the dilatometric method was employed. The dilatometer contained *m*-xylene as the indifferent fluid, and the long stem was surrounded by the graduated tube of a burette which served as a scale and also protected the capillary from fluctuations of temperature. The instrument was immersed in a thermostat at a definite temperature, and after allowing 15 minutes for the apparatus to assume this temperature, the movement of the meniscus was observed.

For short periods of time there was no appreciable movement

at any given temperature, but with longer periods the following results were obtained :

Temp.	Time (hrs.).	Variation in level of fluid.	Variation per hour.
29·3°	24	−0·60	−0·025
21·6	26·5	−0·55	−0·020
19·0	24	−0·35	−0·014
17·0	24	+0·20	+0·008
13·5	21	+0·50	+0·024

It will thus be seen that a simple interpolation gives the equilibrium temperature as 17·7°, which agrees with the transition point indicated by the break in the solubility curve.

The cooling curves of solutions of potassium ferrocyanide of various concentrations over the range 24—13° were found to be quite smooth.

The iron content of a number of samples of crystals, grown at 0° and at temperatures somewhat above 30°, has been determined. The crystals were dried for varying periods between absorbent material under a uniform pressure of 4 lb.; it was found that the composition remained constant after 24 hours. In all cases the results were the same, the iron content approximating to that required by the trihydrate. Further, no differences could be detected in the crystalline form of crystals grown at temperatures above and below the transition point; no crystallographic measurements have been made, however.

Table III shows the densities of the saturated solutions and the solubilities as interpolated at even temperatures.

TABLE III.

		G. of $K_4Fe(CN)_6$				G. of $K_4Fe(CN)_6$	
Temp.	$D^{t°}_{4°}$.	in 100 g. H_2O.	in 100 g. sol.	Temp.	$D^{t°}_{4°}$.	in 100 g. H_2O.	in 100 g. sol.
7·5°	—	19·19	16·10	*17·7°*	*1·1471*	*27·62*	*21·64*
10·0	—	21·00	17·36	20·0	1·1543	28·02	21·89
15·0	1·1378	24·25	19·52	25·0	1·1701	31·53	23·97

Summary.

1. Various methods of estimating alkali ferrocyanides have been critically examined, and a new process, involving the conversion of the ferrocyanide to the ferric condition by means of concentrated sulphuric and nitric acids, is described. This method is shown to be accurate and suitable for use in solubility determinations. It may also be used for the estimation of ferricyanides.

2. The solubilities of potassium ferrocyanide in water at temperatures up to 25° have been determined and represented by a curve.

A break in the latter indicates a change in the solid phase, the transition point being about 18°.

3. The densities of saturated solutions of the salt have been determined, and the density curve shows a slight change in direction above 17°.

4. By the dilatometric method, the transition point between the two phases is established at 17·7°.

5. Crystals of the salt grown above and below the transition point did not exhibit any apparent difference in crystalline form or in the degree of hydration.

The author wishes to express his indebtedness to Dr. J. Newton Friend for his constant help and interest in this research.

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CLXXXVII.—*Selective Solvent Action. Part VI. The Effect of Temperature on the Solubilities of Semi-solutes in Aqueous Alcohol.*

By ROBERT WRIGHT.

THE formation of complexes between its constituents has frequently been assumed to account for the deviation of certain physical properties (*e.g.*, viscosity, refractive index, and density) of aqueous alcohol from those calculated from the mixture rule. If such solvates exist, then it may be expected that rise of temperature will decrease the extent of solvation, since, as a rule, complexes dissociate at higher temperatures. Such a decrease in solvation should affect the solvent power of the mixed solvent for a semi-solute. For example, if 50% aqueous alcohol at 100° contains a higher proportion of free (desolvated) alcohol and water than the same mixture at 20°, this increase in the amount of free water and alcohol should cause an increase in the solubility of a water-soluble salt, or of an alcohol-soluble organic substance. Such an increase in solubility is distinct from the ordinary increase in solubility which takes place in a simple solvent with rise of temperature. In Table I are given the solubilities of five salts (none of which crystallises with water of crystallisation) at 20° and at 100°, both in water and in 50% (by weight) aqueous alcohol. The ratio of the solubilities at the two temperatures is also given for each salt both in water and in the mixed solvent. It will be seen that the ratio is always greater for the mixed solvent than for pure water. If the extent of water–alcohol solvation remained the same at 100° as at 20° there would be the same pro-

portion of free water at the two temperatures, and consequently the ratio of the solubilities of a salt at the two temperatures should be the same for the mixed solvent as it is for pure water. Since this ratio is always greater in the case of the aqueous alcohol, it is concluded that rise of temperature tends to decompose the water–alcohol complexes, this increase in free water producing the abnormal increase in salt solubility.

TABLE I.

Solubilities of salts in water and in 50% (by weight) aqueous alcohol at 20° and 100°.

(G. of solute per 100 g. solvent.)

	Water, 20°.	Water, 100°.	Ratio, 100°/20°.	50% EtOH, 20°.	50% EtOH, 100°.	Ratio, 100°/20°.
NaCl.	36·0	39·1	1·09	9·8	12·1	1·24
	36·0	39·1		9·8	12·1	
KCl.	34·3	56·5	1·64	6·0	15·3	2·55
	34·3	56·0		6·0	15·3	
$KClO_3$.	7·2	56·8	7·84	1·1	14·0	12·8
	7·2	56·0		1·1	14·2	
K_2SO_4.	11·1	23·9	2·15	0·15	0·51	3·64
	11·2	24·1		0·13	0·51	
$Ba(NO_3)_2$.	9·1	33·5	3·69	1·0	4·7	4·65
	9·1	33·6		1·0	4·6	

The solubilities of potassium nitrate in aqueous alcohol of varying composition at 20° and 60° are given in Table II, the values being taken from Seidell's solubility tables. The ratio of the solubilities at the two temperatures is given in each case and it will be seen that it is always greater for aqueous alcohol, of whatever composition, than for pure water. Judging from the values of the ratios, the desolvation with rise of temperature would seem to be greatest with alcohol of about 20% strength. It is obvious that aqueous alcohol which contains only a small proportion of one component, whether alcohol or water, will on desolvation only slightly alter the amounts of its free constituents. Hence the values of the ratios for 90% alcohol and for 5% alcohol are nearer the ratio given by pure water than are those for alcohol–water mixtures of intermediate strength.

TABLE II.

Solubility of potassium nitrate in aqueous alcohol of various concentrations.

(G. per 100 g. solvent.)

Alcohol, %	0	5·5	9·4	13·6	19·1	30	40	60	90
20°	31·6	24	20	16	11	7	5	2	0·3
60°	110	93	79	69	52	31	21	8	1·1
Ratio	3·48	3·87	3·95	4·31	4·72	4·43	4·20	4·00	3·67

For alcohol-soluble solutes, the same result was obtained, but here it was necessary to take into consideration the solubility of the substance in water, which was never negligible, and, in the case of succinic acid, was comparable with that in alcohol. In Table III are given the solubilities at 20° and 30° of four substances in water, alcohol, and the 50% mixture. The ratio of the solubilities at the two temperatures is also given in each case both for the mixed and for the unmixed solvents; with the unmixed solvents the sum of the solubilities is used in calculating the ratio. Again it will be seen that the increase of solubility is always greater with the mixed solvent.

It is thus obvious that a considerable amount of desolvation of the aqueous alcohol takes place with rise of temperature, although it is not possible to calculate the exact extent of such a change. It is, however, not complete at 100°, for in such an event the alcohol would have no effect on the solvent power of water, and the solubility of a salt in 50% alcohol would be simply half of its solubility in pure water.

TABLE III.

Solubilities of some organic substances in water, alcohol, and 50% (by weight) aqueous alcohol, at 20° and 30°.

(G. of solute per 100 g. solvent.)

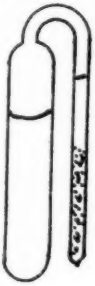
Solvent.	Succinic acid.	Benzoic acid.	Salicylic acid.	Acetanilide.
		At 20°.		
Water.	6·8	0·34	0·21	0·53
	6·7	0·35	0·23	0·52
Alcohol.	10·0	53·0	51·0	28·8
	10·1	52·0	52·0	28·8
50% EtOH.	13·6	17·0	11·8	11·9
	13·8	16·9	11·8	11·9
		At 30°.		
Water.	10·5	0·41	0·30	0·70
	10·4	0·43	0·32	0·72
Alcohol.	12·0	66·0	57·0	40·7
	11·8	65·6	57·5	40·3
50% EtOH.	20·8	25·4	17·9	18·9
	21·0	25·0	18·0	18·7
		Ratios of solubilities, 30°/20°.		
Unmixed solvents.	1·33	1·25	1·11	1·42
Mixed solvents.	1·52	1·48	1·52	1·58

EXPERIMENTAL.

The solubilities at 20° and 30° were determined in the usual manner. The saturated solutions were prepared in stoppered tubes in a thermostat, weighed portions were taken, and the amount of

solute was estimated either by titration or by evaporation to dryness. In the case of acetanilide, the evaporation was carried out under reduced pressure at 40°. At 100°, in addition to the usual necessity of obtaining a saturated solution free from excess of suspended solute, care had to be taken to guard against alteration in the composition of the mixed solvent by evaporation. The method of carrying out a determination was as follows. To a test-tube of 10 mm. diameter and 5 c.c. capacity was sealed a 20 cm. length of tubing about 4 mm. in diameter. After cleaning and drying, a sufficient quantity of dry salt was placed in the tube and about 3 c.c. of solvent were added by means of a pipette, care being taken to avoid wetting the walls of the narrower tube. This tube was then bent round until it lay parallel with the test-tube (see Fig. 1), and was finally sealed off as shown, the whole forming a U with one limb wider than the other. The sealed tube was rocked in a bath at 100° for 4 hours until saturation was complete. It was then held in a special pair of tongs, and, while still under the boiling water, was manipulated so that the excess solid was brought into the narrow limb, the wide limb being left about three-quarters full of the clear saturated solution. The tube was now removed from the bath and allowed to cool to room temperature; part of the salt crystallised during the cooling, but as the tube was sealed no alteration in the composition of the solvent could take place. The wide limb was cut off above the level of the solution and weighed with its contents, and the solubility of the salt was found by evaporation to dryness and a second weighing.

FIG. 1.



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CLXXXVIII.—*The System Lead Chloride–Lead Iodide–Water.*

By ARTHUR LINDSAY MCRAE SOWERBY.

THE literature yields only the most conflicting and unsatisfactory accounts of double salts of the type $x\mathrm{PbCl_2},y\mathrm{PbI_2}$, and a systematic investigation of their stability and properties was therefore undertaken.

Various workers (*e.g.*, Dietzell, *Dingler's Poly. J.*, 1868, **190**, 41; Field, J., 1893, **63**, 540) have prepared salts to which they ascribed formulæ of this type, without sufficient evidence that they were true double salts. Herty (*Amer. Chem. J.*, 1896, **18**, 290) claims

to have shown that these substances were not true chemical compounds, but isomorphous mixtures of lead chloride and lead iodide; and later (Herty and Boggs, *ibid.*, 1897, **19**, 820), he concluded that "all the evidence thus far obtained tends to show that lead iodide and lead chloride will crystallise together, the lead chloride being in excess."

Thomas (*Compt. rend.*, 1898, **126**, 1349), reviewing previous work in conjunction with his own, concluded that PbICl could exist as a true compound.

Two-component Systems.

To the system lead iodide–lead chloride–water there correspond three two-component systems, *viz.*, each salt and water, and the two salts only. The first two systems show no points of particular interest within the temperature range over which they have been investigated (0—100°); in neither case is there any report of a hydrate, and the solubility is sufficiently small to make the temperature of the eutectic point approximate closely to that of pure water. At high temperatures, there is considerable hydrolysis, however, and the two-component systems lead chloride–water and lead iodide–water become special cases of the three-component systems lead oxide–water–hydrochloric or hydriodic acid, the solubility curves really representing the locus of the isothermal invariant points where lead hydroxide or a basic salt exists as a solid phase beside the normal salt.

The binary system lead iodide–lead chloride was investigated by Mönkemayer (*Neues Jahrbuch für Mineralogie*, Beilageband, 1906, **22**, 1) who concluded that it belonged to Roozeboom's Type V of mixed crystals (Roozeboom, *Z. physikal. Chem.*, 1899, **30**, 403). The evidence upon which he based this conclusion appears to be insufficient; he observed the rate of cooling of fused mixtures of the two salts, and by plotting the time of the eutectic halt against composition, and extrapolating to zero eutectic halt, he obtained values for the limiting compositions of the mixed crystals. On re-plotting the figures given by Mönkemayer and extrapolating as described, the limiting compositions appear to be 100% $PbCl_2$ and 100% PbI_2, respectively. There is no other evidence in the paper of the formation of mixed crystals, nor is any compound formed at these temperatures. It is therefore very doubtful whether the relations are not those of the simplest possible two-component system—two melting-point curves meeting in a eutectic point at 306°.

Experimental.

All results were obtained by the analysis of solutions and solids which had been allowed to attain equilibrium in a thermostat, the

analysis normally comprising a volumetric estimation of total halides by Volhard's method and an independent estimation of iodide by another method. Since in all cases the concentration of chloride was high compared with that of iodide, the errors in determining the former by difference are not appreciably greater than if the chloride had been directly determined.

Determination of Iodide.—The determination of the iodide in presence of a large excess of chloride offered considerable difficulty, especially as the concentration of lead iodide never exceeded 0·09 g. per 100 c.c. of solution (corresponding to less than 0·05 g. of iodine per 100 c.c.).

Of the many methods tried and abandoned, two only are of interest. The first depends upon the statement of Pisani (Fresenius, "Quantitative Analysis," Sixth Ed., 444) that if silver nitrate solution be run into a solution containing mixed iodides and chlorides to which have been added a few c.c. of starch iodide solution of known silver value, the metallic iodide is first precipitated, and next the iodine from the starch iodide, thus giving an end-point before the chlorides begin to be precipitated. On trial with very dilute solutions, using the equivalent of 0·05 c.c. of $N/10$-solution of iodide for each titration and $N/1000$-silver nitrate, it was found that this statement is correct, provided that the chloride concentration is not much greater than that of the iodide. In the presence of a large excess of chloride, however, the end-point was delayed, the quantity of silver nitrate required increasing by about 40% as the chloride concentration was increased up to about 100 times that of the iodide. For analysis of the solutions in the present work, this method was therefore valueless, but it was found convenient for the analysis of the solids, of which only small amounts were available. Trustworthy results were obtained, provided that (*a*) the normality of the chloride was not more than double that of the iodide, (*b*) the total volume of the solution being titrated was kept constant in all cases, and (*c*) the silver nitrate solution was standardised against an iodide solution of known concentration under operating conditions.

The second method that proved unsuccessful in its original form is due to Benedict and Snell (*J. Amer. Chem. Soc.*, 1903, **25**, 1139); in this method, the iodine is liberated by iodate and acetic or nitric acid, and extracted with carbon disulphide. The resulting pink solution is washed and titrated with thiosulphate. Three difficulties, all due to the extreme smallness of the amount of iodide to be measured, were encountered:

(*a*) The acetic acid available (ordinary laboratory reagent) appeared to re-absorb, by some secondary reaction, the iodine at

first liberated, so that the results obtained depended on the length of time that elapsed between the liberation and the final extraction, and were invariably low, although not by a constant amount. Nitric acid of ordinary purity was free from this objection, and was consequently used for further experiments.

(*b*) The carbon disulphide used reacted with iodine slowly, the titration value of the solution falling to about one-half in 15 hours, but carbon tetrachloride proved to be satisfactory and was used throughout.

(*c*) The very dilute solution (approx. 0·005*N*) of thiosulphate used gave erratic variations of the order of 20% in the titrations. Every attempt to eliminate this source of error failed completely, and solutions of arsenious oxide gave rise to similar variations.

Finally, a colorimetric method, based on the method of Benedict and Snell, was adopted : Ten c.c. of the solution to be examined were diluted with a little water to prevent crystallisation, and the lead was precipitated as sulphate and filtered off. Filtrate and washings were made up to 300 c.c. in a separating funnel. A known volume of a standard lead iodide solution was made up to the same volume in a second funnel. The iodine was then liberated in both funnels by the addition of potassium iodate and nitric acid, extracted with carbon tetrachloride, and the two resulting solutions were made up to the same volume in small standard flasks. These solutions were then matched in a Dubosc colorimeter, illuminated preferably by daylight. From the colorimeter readings and the known concentration of one solution, that of the other could readily be calculated. This method was found to be accurate to within 2%, even in estimating no more than 0·5 mg. of iodine.

Results.

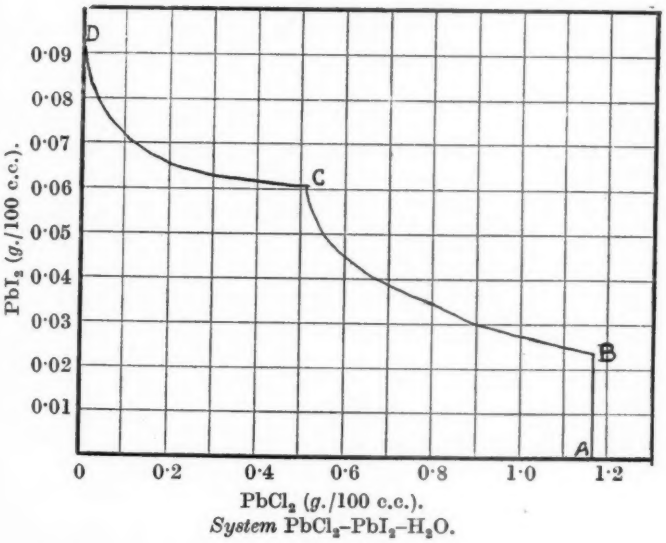
Table I and Fig. 1 summarise the results obtained at 30°. The letters in the first column of the table refer to the corresponding points in the diagram. The points B and C are isothermal invariant points. The continuity of the curve BC is evidence of the existence of only one solid over this range of concentrations. Analysis of the solid obtained from solutions represented by the curve BC was attempted, but the quantity obtained was so small as to preclude accuracy.

In order to obtain larger quantities of this solid, the necessary quantities of lead iodide and lead chloride were boiled with water until they dissolved, and the solution was allowed to come to equilibrium in the thermostat. A sample of the solution was then withdrawn and analysed for total halides in order to determine with sufficient accuracy the point on the curve to which the solution

TABLE I.

	Solution. PbI_2 (g./100 c.c.).	Solution. $PbCl_2$ (g./100 c.c.).	Solid phase.
A.	—	1·171	$PbCl_2$
	0·0081	1·171	,,
	0·0120	1·171	,,
	0·0168	1·171	,,
B.	0·0235	1·171	$PbCl_2$ & PbICl
	0·0241	1·140	PbICl
	0·0277	0·969	,,
	0·0278	0·958	,,
	0·0334	0·820	,,
	0·0390	0·717	,,
	0·0421	0·631	,,
	0·0432	0·631	,,
	0·0520	0·550	PbICl
	0·0531	0·545	,,
C.	0·0602	0·518	PbICl & PbI_2
	0·0606	0·417	PbI_2
	0·0620	0·352	,,
	0·0630	0·270	,,
	0·0647	0·209	,,
	0·0687	0·144	,,
	0·0712	0·100	,,
	0·0788	0·046	,,
D.	0·091	—	,,

FIG. 1.



System $PbCl_2$–PbI_2–H_2O.

corresponded. Larger amounts of solid, often as much as 0·5 g., were thus obtained. These solids were analysed, after drying, by Volhard's method for total halides, and by Pisani's method (see above) for iodide. As a check, chlorides were estimated again after liberating and boiling off the iodine. No attempt was made to estimate lead in the solid, since the boiling involved in its preparation caused a small amount of basic salt to be formed. The results are summarised in Table II, and it is seen that the solid in equilibrium with solutions having the concentrations expressed by the curve BC is PbICl. No other compounds are formed at this temperature.

TABLE II.

Solution.		Solid.		
$PbCl_2$ (g./100 c.c.).	PbI_2 (g./100 c.c.).	$PbCl_2$ (equivs./100 g.).	PbI_2 (equivs./100 g.).	Ratio $PbI_2 : PbCl_2$.
0·86	0·032	0·271	0·265	0·978
0·765	0·036	0·268	0·269	1·004
0·67	0·041	0·270	0·271	1·004
0·56	0·051	0·269	0·268	0·996

A line drawn from the origin of Fig. 1 through the points corresponding to solutions containing lead iodide and chloride in equimolecular quantities does not cut the solubility curve, BC, of lead chloroiodide, but the curve CD. In accordance with this, it is found that the double salt is decomposed by water at the temperature of the isotherm.

An attempt was made to determine the isotherm for 70°, but hydrolysis was so considerable that the work was abandoned.

Summary.

The isotherm for 30° in the system lead chloride–lead iodide–water has been completely investigated. Three solubility curves have been found, corresponding to the two salts and to the binary compound PbICl. This salt has been shown to be decomposed by water, and the composition of solutions with which it can remain in equilibrium has been determined.

Methods have been developed by which small amounts of iodide can be estimated in presence of chloride.

The author's thanks are due to Professor F. G. Donnan for his kindly interest in the work, and to the late Miss K. A. Burke for many valuable suggestions in connexion with methods of analysis.

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CLXXXIX.—*The Ternary System Barium Iodide–Iodine–Water and the Formation of Polyiodides.*

By A. C. D. RIVETT and JOHN PACKER.

VARIOUS attempts have been made to define the equilibrium relations existing between polyiodides and their constituents and to assign formulæ to the former. That a tri-iodide, such as that of potassium or barium, may exist in solution is very generally assumed.

Clark and Duane (*Physical Rev.*, 1922, **20**, 85), in fact, claim to have made a detailed examination by *X*-ray methods of the crystal structure of potassium tri-iodide, but they do not state how the salt was prepared. Many others have failed to obtain it: neither from aqueous solution (Parsons and Whittemore, *J. Amer. Chem. Soc.*, 1911, **33**, 1933) nor from 60 or 40% alcoholic solutions (Parsons and Corliss, *ibid.*, 1910, **32**, 1367) can any solid polyiodide of potassium be isolated. From thermal examination of the binary system potassium iodide–iodine, Kremann and Schoulz (*Monatsh.*, 1912, **33**, 1081) concluded that KI_4, highly dissociated, existed in the fusion, but they could find no evidence for the presence of a polyiodide poorer in iodine. According to Abegg and Hamburger (*Z. anorg. Chem.*, 1906, **50**, 403), no polyiodide of potassium of less complexity than KI_7 exists.

Pearce and Eversole (*J. Physical Chem.*, 1924, **28**, 245) obtained results in dilute solutions of barium iodide, unsaturated with iodine, which were fairly consistent with a supposition of the presence of tri-iodide; but in *M*-solutions and upwards, saturated with iodine, they considered that pentaiodide was formed. From measurements of conductivities, viscosities, migration numbers, distribution coefficients, and other properties, usually over very limited ranges of concentration, other authors have obtained indications of polyiodides to which, on more or less satisfactory grounds, they have been able to assign formulæ.

In order to obtain quantitative information over a much wider range of temperature and concentration of components than has yet been recorded, the system barium iodide–iodine–water has been investigated between — 15·8° and 90°. Barium iodide (B.D.H.), recrystallised from water as the hydrate $2BaI_2,15H_2O$, and lower hydrates obtained by heating, were used with resublimed iodine (A. R.) and water in the preparation of suitable complexes. These were rotated in sealed tubes in a thermostat at the required temperature from 0° to 90° until equilibrium was attained. Shorter times, with only intermittent stirring and shaking, were given at — 15·8°, the temperature being maintained by means of ammonium chloride and ice. Solutions were drawn off into pipettes through cotton-wool plugs, any iodine removed by reaction with the cotton being negligible. Iodine was estimated by direct titration of one sample with thiosulphate, whilst in another sample, from which the iodine had been completely removed by evaporation, the iodide was estimated volumetrically against silver nitrate with thiocyanate as indicator. At 0° and 25° the usual " rest " method was employed to give information as to the composition of the solid phase. At lower and higher temperatures the wet solid was not readily separ-

ated without alteration of composition. The initial complex was therefore carefully synthesised and its composition used instead. Provided that the complex is not very near in composition to the saturated solution, this method is fairly accurate.

Table I contains the results at 0° and 25°, and Table II those at − 15·8°, 50°, 75·2°, and 89·9°. Compositions are given in % by weight, those of water (not given) being obtainable by difference. In the last column hydrates are specified by figures in parentheses, giving first the number of barium iodide molecules, and secondly the number of water molecules.

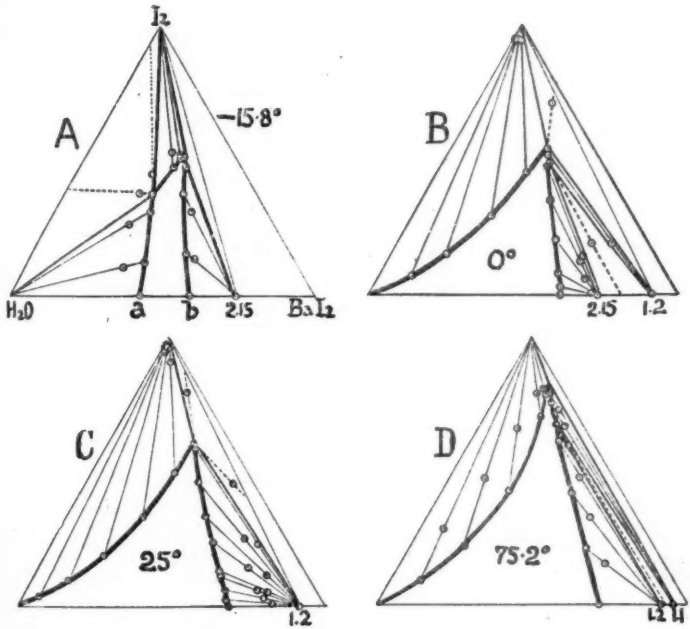
TABLE I.

		Composition, % by weight.				
		Solution.		Wet solid.		
Temp.	D_4°.	BaI_2.	I_2.	BaI_2.	I_2.	Solid phases.
0° ± 0·05°	1·169	10·5	7·4	0·6	94·9	Iodine.
	1·365	17·9	15·2	1·1	94·6	,,
	1·780	25·5	29·5	1·8	94·7	,,
	2·415	29·0	45·4	3·0	94·1	,,
	—	31·4	54·0	24·3	71·0	Iodine and (1, 2).
	—	32·7	51·8	69·8	19·0	(1, 2).
	—	34·6	49·4	63·0	19·2	(1, 2) and (2, 15).
	—	35·1	47·7	62·8	14·2	(2, 15).
	2·561	41·7	35·1	62·7	12·5	,,
	2·322	50·4	20·3	66·9	6·2	,,
	2·167	57·7	8·2	72·3	1·0	,,
	2·108	60·7	3·0	72·2	0·5	,,
	2·071	62·5	0·0	—	—	,,
25° ± 0·02°	1·081	5·8	3·7	0·1	96·7	Iodine.
	1·214	12·4	10·0	0·4	97·3	,,
	1·436	19·3	19·5	1·2	94·6	,,
	1·827	24·8	33·2	1·5	96·3	,,
	—	26·6	50·0	4·9	90·8	,,
	—	27·2	61·1	16·3	79·7	Iodine and (1, 2).
	—	27·6	60·9	47·3	45·9	,, ,,
	—	28·8	58·6	66·8	23·4	(1, 2).
	—	36·4	46·8	61·4	25·3	,,
	—	44·8	33·8	75·6	11·5	,,
	—	52·0	24·0	68·0	14·2	,,
	2·405	59·7	13·3	78·9	5·2	,,
	—	60·6	11·7	75·0	6·2	,,
	2·339	64·3	6·5	78·5	3·1	,,
	2·31	66·7	2·7	82·8	0·9	,,
	2·277	68·8	0·0	—	—	,,

From these tables and the triangular diagrams, the succession of changes may readily be followed. At − 15·8° (Fig. 1A) there are three curves, the solids being ice, iodine, and the hydrate (2, 15). At − 33·5°, the eutectic temperature of the binary system barium iodide–water (Packer and Rivett, J., 1926, 1061), the points *a* and *b* coincide, and below it all liquid phases are ternary in composition. A little below 0° the hydrate (1, 2) appears, and there are then four solubility curves. At 0° (Fig. 1B) the ice curve vanishes and the

system is one showing three solids, iodine, (1, 2), and (2, 15). The latter hydrate cannot exist above 25·7°, and for a considerable temperature range beyond this the system is a simple one of two curves, as in Fig. 1C, the solids being iodine and (1, 2). Actually at 25°, for which this figure holds, there must be still a very small curve of (2, 15), but this has been omitted. The relations between compositions of solutions and "rests" at 25° give proof that the highest hydrate is (2, 15), and not either (1, 7) or (1, 6), as has been commonly assumed (compare Packer and Rivett, *loc. cit.*, p. 1062).

FIG. 1.



The temperature at which the hydrate (1, 1) first occurs in the ternary system could not be determined accurately by the thermometric method, but at 75·2° its solubility curve is as shown in Fig. 1D: that of (1, 2) vanishes at 98·9°.

Apart from the fact that no solid polyiodide is obtained, the interest of the system lies in the solubilities attained by iodine. In Table III are set out figures for the iodine saturation curves, compositions of solutions being given in equivalents per 1000 g. of water. In the last column is given the ratio of iodine atoms to iodide ions in solution. The amount of combined iodine is presumably the total found by titration with thiosulphate less that merely dissolved in the water. The amount of the latter cannot be

Table II.

Temp.	Composition, % by weight. Solution. BaI_2.	Solution. I_2.	Initial complex. BaI_2.	Initial complex. I_2.	Solid phases.
−15·8° ± 0·1°	43·5	—	—	—	Ice.
	38·7	12·7	32·5	10·6	,,
	31·4	31·3	26·7	26·8	,,
	28·5	37·6	24·3	38·2	Ice and iodine.
	28·7	37·6	24·9	45·4	,, ,,
	30·8	47·5	27·1	53·3	Iodine.
	31·2	50·8	30·2	52·5	,,
	32·2	51·4	34·6	47·8	Iodine and (2, 15).
	38·7	37·6	44·4	31·4	(2, 15).
	50·4	15·9	54·1	13·5	,,
50° ± 0·02°	11·0	10·1	8·1	24·6	Iodine.
	19·9	24·9	14·3	42·2	,,
	24·5	47·2	18·6	57·2	,,
	22·1	68·3	21·5	69·4	,,
75·2° ± 0·05°	9·4	9·8	7·4	28·5	Iodine.
	17·0	23·0	11·6	47·0	,,
	21·4	42·5	12·7	65·6	,,
	18·0	70·0	12·8	78·5	,,
	15·7	77·6	14·1	79·8	,,
	14·3	82·0	—	—	Iodine and (1,1) (extrap.).
	16·8	78·3	22·6	72·4	(1, 1).
	18·9	74·9	27·2	66·3	,,
	24·2	67·2	32·2	59·3	(1, 1) and (1, 2).
	28·6	60·7	42·1	47·4	(1, 2).
	41·8	41·6	52·3	32·7	,,
	56·6	21·0	65·3	15·7	,,
89·9°	12·8	83·4	8·9	88·0	Iodine.
	14·7	75·3	9·7	83·2	,,

Table III.

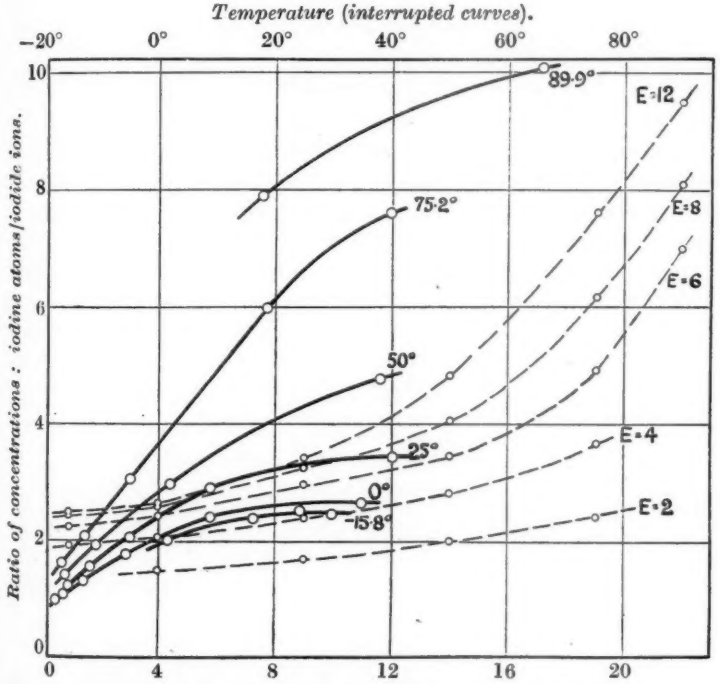
(Solutions saturated with iodine.)

Temp.	Equivs. per 1000 g. H_2O. BaI_2.	I_2.	Ratio $I_2 : BaI_2$.	Temp.	Equivs. per 1000 g. H_2O. BaI_2.	I_2.	Ratio $I_2 : BaI_2$.
−15·8°	4·35	8·79	2·02	50°	0·70	1·00	1·42
	7·27	17·28	2·38		1·84	3·54	1·93
	8·88	22·28	2·51		4·42	13·13	2·97
	9·99	24·59	2·46		11·65	55·5	5·55
0°	0·65	0·71	1·09	75·2°	0·59	0·95	1·61
	1·37	1·79	1·31		1·45	3·02	2·08
	2·90	5·16	1·78		3·04	9·29	3·06
	5·79	13·97	2·41		7·71	46·2	5·99
	11·0	29·1	2·65		11·98	91·3	7·62
25°	0·33	0·32	0·98	89·9°	7·52	59·3	7·9
	0·82	1·015	1·24		17·2	173·0	10·1
	1·61	2·51	1·56				
	3·02	6·23	2·06				
	5·81	16·84	2·90				
	12·08	41·4	3·43				

accurately estimated without making more or less arbitrary assumptions: in any case it will be small compared with the total iodine concentrations in the cases examined.

Fig. 2 contains two sets of curves which illustrate these results. The continuous lines are isotherms showing the ratio of iodine atoms to iodide ions plotted against equivs. of iodide per 1000 g. of water. At first they are not far from straight lines, but later they flatten, and at the lower temperatures seem to reach maxima. Throughout, the more iodide present, the more iodine is taken up per equiv. of iodide. In very dilute solutions at all temperatures the ratio of atoms to ions approximates to unity (compare Pearce and Eversole,

FIG. 2.



loc. cit., p. 252), and then with increase of salt concentration it rises the more rapidly the higher the temperature. From these curves have been obtained by interpolation the values of the ratio of atom to ion at different temperatures for barium iodide concentrations of 2, 4, 6, 8, and 12 equivs. per 1000 g. of solvent, and in Fig. 2 the interrupted curves show for each of these concentrations the values of the ratios plotted against temperature. The higher the temperature the more iodine is added per equiv. of iodide, and the rate of increase is greater the greater the iodide concentration. Supposing all the iodine to be distributed evenly amongst the iodide

radicals, the composition of the polyiodide radical ranges from I_2' to I_{11}', and at temperatures above the highest investigated, 89·9°, still greater amounts of iodine would certainly be taken up.

Attempts to apply the mass action law in systems like these cannot be expected to succeed; and there seems no reason to suppose that the formation of any one polyiodide represents the sole action at any particular stage. A glance at the continuous curves of Fig. 2 shows how in the less concentrated solutions of barium iodide the ratio of iodine to iodide approximates to 2, corresponding with an ion I_3'. Over selected ranges of iodide concentration one can interpret the results in terms of this or of numerous higher polyiodides.

It is clear that iodination is progressive, increasing in extent per iodide ion with increase of concentration of the latter and with rise of temperature. Whether the temperature effect is due solely to increase of concentration, and hence mass effect, of the iodine in the water present, cannot be stated. One might expect a polyiodide to become more unstable and to dissociate with rise of temperature. It may be that the apparent increase of stability with rise of temperature is due to the fact that the formation of polyiodide is not an addition of iodine molecules to a simple iodide ion, I′, but is a replacement by iodine of the water molecules which the simple ion may attach to itself in numbers sufficient to constitute it a full co-ordination complex. Thus we should have

$$I',xH_2O + yI_2 \rightleftharpoons I',(x-y)H_2O,yI_2 + yH_2O.$$

If hydration and iodination of the ion are both exothermic reactions, but the former more so than the latter, rise of temperature will displace the equilibrium to the side of the latter, other things being equal. In dilute solution the tendency would be for the reaction to go to the left.

Summary.

1. The ternary system barium iodide–iodine–water has been fully examined at − 15·8°, 0°, 25°, and 75·2°, and partially at 50° and 89·9°.

2. The hydrate $2BaI_2,15H_2O$ has been shown to exist, but neither a hexa- nor a hepta-hydrate has been found. No solid polyiodides have been formed.

3. Assuming the iodine present in solution to be attached to the anion, the mean compositions of the polyiodides present in the solutions examined range up to $BaI_2,10I_2$ at 90°; and at higher temperatures the iodine content will be still greater.

4. For a constant water content of solution, the ratio of iodine to iodide increases with increase of iodide concentration; it also

increases with temperature for a constant iodide concentration. Both facts are explicable if the action be regarded as a replacement of water in a hydrated iodide ion by iodine, the heat of reaction of a simple ion with water being greater than that with iodine, so that the substitution of the latter for the former is endothermic.

UNIVERSITY OF MELBOURNE. [*Received, April 11th*, 1927.]

CXC.—*The Union of Benzoylacetonitrile with Organic Bases in the Presence of Salicylaldehyde. Part I.*

By PANCHAPAKESA KRISHNAMURTI and BIMAN BIHARI DEY.

SALICYLALDEHYDE and benzoylacetonitrile condense together in the presence of a few drops of piperidine to give a poor yield of 3-benzoylcoumarin (Krishnamurti and Dey, *Proc. 13th Ind. Sci. Cong.*, 1926); at the same time there is produced a *base*, $C_{14}H_{18}ON_2$. This base is obtained in good yield when piperidine and benzoylacetonitrile react together in molecular proportion in the presence (but not otherwise) of a few drops of salicylaldehyde. It is a mono-acid base which is stable towards mineral acids, with which it forms characteristic, crystalline salts, and towards boiling dilute aqueous alkalis, but is decomposed by alcoholic potash with the liberation of piperidine. It is converted into piperidine and benzoic acid by the action of alkaline permanganate.

No definite acetyl or benzoyl derivative could be prepared, but the base readily yields a *nitroso-hydrochloride* with hydrochloric acid and sodium nitrite, which is decomposed by sodium bicarbonate to give a bright yellow iso*nitroso*-derivative. This compound readily yields diacyl derivatives, and gives benzoic acid on distillation with 70% sulphuric acid. The original base, when heated above its m. p., is decomposed into its constituents.

That it is the *N*-hydrogen atom of piperidine that takes part in the reaction is shown by the fact that the *N*-alkylpiperidines do not give this reaction. The constitution of the base may therefore be represented by (I) $CH_2Bz{\cdot}C(:NH){\cdot}NC_5H_{10}$ or (II) $CH_2Bz{\cdot}C{:}NH{\cdot}NC_5H_{10}$. Formula (II) is more in accordance with the properties of the base, especially its instability towards heat and its stability towards concentrated acids and towards alkalis. The *iso*nitroso-derivative may be represented thus: (III) $OH{\cdot}N{:}CBz{\cdot}C{:}NH{\cdot}NC_5H_{10}$.

The action of salicylaldehyde as catalyst may be explained by assuming that it first condenses with benzoylacetonitrile in the presence of piperidine to form the salicylidene derivative; the nitrogen atom of the CN group in this then reacts additively with

piperidine by migration of the hydrogen atom of the NH group of the latter; finally, the compound thus produced is hydrolysed, salicylaldehyde being regenerated.

Nitro-, bromo-, and *p*-methoxy-salicylaldehydes—and also β-naphtholaldehyde, but to a lesser extent—similarly act as catalysts, whereas the reaction fails with *o*-methoxybenzaldehyde and *m*- and *p*-hydroxybenzaldehydes, which do not contain the necessary hydroxyl group in the ortho-position to the aldehyde group.

EXPERIMENTAL.

The Base (II).—A mixture of benzoylacetonitrile (1 mol.), piperidine (2 mols.), salicylaldehyde (2—3 drops), and absolute alcohol (50 c.c.) was heated under reflux for about 3 hours. A portion of the alcohol was then distilled off, and the reddish-brown solution was diluted with much water, mixed with concentrated hydrochloric acid (5 c.c.), and, after 12 hours, decanted from the resinous matter and treated with excess of sodium hydroxide. The thick, white precipitate, after being washed, crystallised from alcohol in colourless, rectangular prisms, m. p. 173° (yield, about 80%). The base is insoluble in water, ether, or petroleum, and easily soluble in benzene, alcohol, acetone, chloroform, or dilute acids; from the last it is precipitated unchanged by alkalis (Found: C, 72·85; H, 8·0; N, 12·2. $C_{14}H_{18}ON_2$ requires C, 73·0; H, 7·8; N, 12·2%).

When heated, the base first melted to a clear liquid and then boiled, piperidine being evolved; the residue was charred and insoluble in acids.

A suspension of the base (0·5 g.) in 2% sodium hydroxide solution (50 c.c.) was slowly treated with potassium permanganate (3 g.); subsequent boiling produced a copious evolution of piperidine. The liquid, after being concentrated and acidified, gave a good yield of benzoic acid, m. p. 121°.

The *hydrochloride* slowly crystallised from dilute hydrochloric acid (1 : 1) in broad, glistening plates, m. p. 235—242° (Found: Cl, 13·2. $C_{14}H_{18}ON_2,HCl$ requires Cl, 13·3%). The *chloroplatinate* formed orange crystals (Found: Pt, 22·6. $2C_{14}H_{18}ON_2,H_2PtCl_6$ requires Pt, 22·4%). The *picrate*, obtained as an oil which solidified slowly, crystallised from alcohol in yellow, glistening prisms which lost alcohol of crystallisation at 98° and melted to a clear liquid at 138°.

The iso*Nitroso-derivative* (III).—The sparingly soluble *hydrochloride* was obtained by adding a dilute solution of sodium nitrite to a solution of the base in dilute hydrochloric acid. After recrystallisation from very dilute alcohol it melted at 258° (decomp.) (Found:

N, 14·2. $C_{14}H_{17}O_2N_3$,HCl requires N, 14·2%). When warmed with a little water and a slight excess of sodium bicarbonate, it gave the *isonitroso*-compound as a bright yellow solid, which crystallised from alcohol in slender needles, m. p. 183° (decomp.) (Found: C, 65·3; H, 6·4; N, 16·15. $C_{14}H_{17}O_2N_3$ requires C, 65·0; H, 6·6; N, 16·2%).

The *dibenzoyl* derivative of (III) was readily prepared by the Schotten–Baumann method. It crystallised from alcohol in clusters of colourless needles, m. p. 148° (Found: C, 72·1; H, 5·3; N, 9·05. $C_{28}H_{25}O_4N_3$ requires C, 71·95; H, 5·35; N, 9·0%). The *diacetyl* derivative, m. p. 180—181° (decomp.), also was easily obtained by heating the base or its hydrochloride with acetic anhydride for a few minutes (Found: N, 12·4. $C_{18}H_{21}O_4N_3$ requires N, 12·35%).

The reactions of benzoylacetonitrile and of other nitriles of the type $CH_2R{\cdot}CN$ with various reactive bases are under investigation.

We wish to thank Prof. C. V. Raman, F.R.S., for giving us facilities for carrying out this work.

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CXCI.—*Melting Points and Heats of Crystallisation of Homologous Series. Part III. Myristic Acid Derivatives.*

By W. E. GARNER and J. E. RUSHBROOKE.

IT has been shown previously (J., 1926, 2491) that the heat of crystallisation of the monobasic fatty acids above C_{10} increases by 2·060 Cal. for every two methylene groups added to the carbon chain; and also that for an even member the heat of crystallisation divided by the absolute melting point increases regularly as the series is ascended. From these two relationships the empirical equation (1) was derived for the melting points of the even members of the monobasic acids:

$$T = (-3{\cdot}61 + 1{\cdot}030n)/(-0{\cdot}0043 + 0{\cdot}002652n) \quad . \quad . \quad (1)$$

where n is the number of carbon atoms in the chain.

If it be assumed that the increment in the heat of crystallisation per methylene group is the same for all homologous series above C_{10}, then an equation of a general character, (2), would be expected to be valid for all series:

$$T = (x + 1{\cdot}030n)/(y + 0{\cdot}002652n) \quad . \quad . \quad . \quad . \quad (2)$$

where x and y are constants depending on the nature of the terminal groups.

In order to check the applicability of equation (2) to any particular series it is necessary to know the value for the heat of crystallisation of one of the even members of the series. In the present investigation, the data necessary for such a test have been procured in the case of the monobasic amides, alcohols, and methyl and ethyl esters. The amides, like the acids, form a series in which the melting points alternate from the odd to the even members, but the alcohols and esters are non-alternating.

The fourteenth member of each of these series was chosen for the test, and the results are in Table I. From the values of x and y in this table, the melting points (*i.e.*, the setting points or equilibrium values) of the members of five homologous series have been calculated and these are given by the continuous lines in the diagram. The experimental values of the melting points culled from numerous sources are shown in the diagram by vertical lines, the length of which indicates their range. The agreement between the calculated and the experimental melting points is within 1—2% and is as good as could be expected in view of the fact that the melting points of homologous series are not known with great accuracy, and that a small change in the constants of equation (2) produces a marked change in the calculated curve.*

TABLE I.

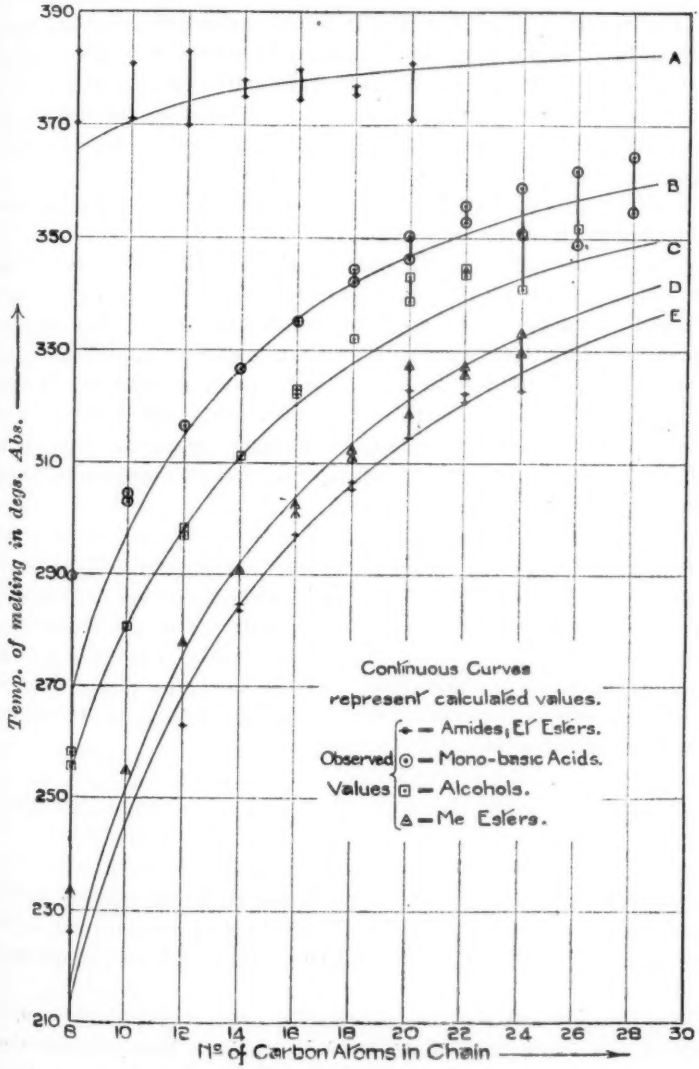
Substance.	Setting point, $t°$.	Q (Cal./mol.).	Q/T.	x.	y.	Heat of cryst. of terminal groups.
I. Alternating series.						
Myristic acid ...	53·7°	10·74	0·03287	−3·68	−0·00426	−1·62
Myristamide ...	103·0	12·92	0·03436	−1·50	−0·00277	+0·56
II. Non-alternating series.						
Methyl myristate	18·35	10·63	0·03647	−3·79	−0·00066	−1·73
Ethyl myristate	11·0	11·17	0·03933	−3·25	+0·00220	−1·19
Myristyl alcohol	37·7	11·76	0·03785	−2·66	+0·00072	−0·60

The melting points as determined by the ordinary method may or may not be identical with the equilibrium values for these temperatures given by the setting points. Partington and Stratton (*Phil. Mag.*, 1924, **48**, 1089) have recorded that the setting point of palmitic acid is lower than its melting point, and we also have observed the same phenomenon with palmitic and eicosoic acids. As Smits has shown ("The Theory of Allotropy," 1922), the melting

* It is desirable that the constants in equation (2) be determined more accurately by measurements of the heats of crystallisation of higher members of the monobasic acid series.

point varies with the rate of heating if equilibrium between the various molecular forms in the liquid or solid states is established slowly. Levene and Taylor (*J. Biol. Chem.*, 1924, **59**, 905) have

FIG. 1.



observed that the melting points of the long-chain fatty acids decrease after the solids have been kept for a long time. This points to slow changes occurring in the solid state and indicates

that the phase equilibria are not established rapidly. It would therefore be expected that the melting points of these substances would vary with the rate of heating, and this would account for the wide range of the experimental values.

The melting points of the alcohols and acids recorded by Levene and Taylor and others for the 18—26th members lie on a curve which is 4—5° higher than the calculated curve. It is not unlikely that this discrepancy is due to the fact that the experimental melting points are not equilibrium values. In the case of the esters, the divergences from the theoretical curve are not large over the whole range from $n = 8$ to $n = 28$.

The agreement is of such a nature as to provide some justification for further work along these lines.

Up to the present, very few quantitative relationships, other than those of a thermodynamical character, have been discovered between the melting points of organic compounds and their other physical properties. This lack of quantitative knowledge applies not only to the melting points but also to other properties which are likewise sensitive to changes in chemical constitution. The factors determining the numerical values of constitutive properties are imperfectly understood and it is difficult to discuss even qualitatively their dependence on chemical constitution.

On account of the similarity which exists between the processes occurring at the melting point and those associated with chemical change, it is not unlikely that the application of the laws of chemical change to melting-point phenomena will yield information of importance for the study of the relationship between melting point and chemical constitution. In the previous paper (*loc. cit.*, p. 2496) a theoretical equation for the melting points of homologous series was deduced along these lines:

$$T = \frac{Q}{4{\cdot}57}\left\{\tfrac{1}{2}(n-2)\log\frac{k_1''}{k_1'} + \log\frac{k_2''}{k_2'} + \log\frac{k_3''}{k_3'} + \log n\right\} \quad . \quad (3A)$$

This equation, which applies only to those homologous series in which no chemical association occurs in the liquid and solid states, contains four variables—the melting point, T, the heat of crystallisation, Q, a number of probability factors, and the number of carbon atoms in the chain, n.

This equation can be expressed in a more convenient form by adopting the conception that for each group in the molecule there is an *equilibrium constant* which determines its distribution between the solid and the liquid phase. This involves making the hypothesis that the groups forming the carbon chain can detach themselves from the surface of the crystal or rejoin the surface independently

of their neighbours. This is rendered highly probable by the possibility of rotation of the groups about the single C—C linkings. There is, however, a limitation to this freedom of movement of individual groups; any group situated between two others, which are themselves attached to the surface, is incapable of movement. Thus the equilibrium constant refers only to those groups which are in such a position that they can move away from or attach themselves to the surface. Of these groups, some will be in the liquid and some in the solid phase. The ratio of those in the solid to those in the liquid phase, or the equilibrium constant, κ, is given by $\kappa = (k''/k')e^{+Q/RT}$, where Q is the heat of crystallisation of the group in question, T is the absolute temperature, and k'' and k' are the probability factors discussed previously (*loc. cit.*). The equilibrium constant of any group will vary with temperature in an analogous manner to the equilibrium constant of chemical change.

According to this view the melting points for long-chain compounds will be given by

$$T = \log_e [\kappa_1^{\frac{1}{2}(n-2)} . \kappa_2 . \kappa_3 . n] \quad . \quad . \quad . \quad . \quad (3B)$$

where κ_1, κ_2, and κ_3 are the equilibrium constants of the methylene group and of the two terminal groups respectively. The value of κ_1 is readily evaluated as follows: For a carbon chain of infinite length, the melting point is 118°; at this temperature, $\kappa_1 = (k_1''/k_1')e^{+Q_1/RT}$, since the probability of attachment of a methylene group at the melting point is equal to the probability of its detachment. The equilibrium constant at any other temperature can readily be calculated from the above equation.

The values of the equilibrium constants of the terminal groups are not yet known, but there is no great difficulty in the way of their determination. A study of the heats of crystallisation of the hydrocarbons and the dibasic acids, together with the data already known, should give these directly.

The application of equation (3B) to the compounds given in Table I is complicated by the fact that the acids are chemically associated to double molecules in the solid and liquid states, whereas the esters occur as single molecules in the solid state (compare Müller and Shearer, J., 1923, **123**, 2043, 3152, 3156). The amides have not yet been investigated by *X*-ray methods, but on account of the similarities between the $-CO_2H$ and $-CO{\cdot}NH_2$ groups and also since the amides and acids give alternating series, it will be assumed that the amides, like the acids, are chemically associated in the solid and liquid states. It is necessary to discuss the alternating and non-alternating series separately.

Alternating Series.—The melting points of alternating series will

be given by a modified form of equation (3A). The molecules are practically twice the length of corresponding members of the non-alternating series, the heat of crystallisation per g.-mol. is doubled, and log n in equation (3A) is replaced by $\frac{1}{2}\log 2n$ in (4A):

$$T = \frac{Q}{4{\cdot}57}\left\{\tfrac{1}{2}(n-2)\log\frac{k_1''}{k_1'} + \log\frac{k_2''}{k_2'} + \log\frac{k_3''}{k_3'} + \tfrac{1}{2}\log 2n\right\} \quad (4A)$$

and

$$T = \log_e\left[\kappa_1^{\frac{1}{2}(n-2)} \cdot \kappa_2 \cdot \kappa_3 \cdot (2n)^{\frac{1}{2}}\right] \quad . \quad . \quad . \quad . \quad (4B)$$

When $n = 14$, the numerical value for the terms in the brackets is 7·18 (for myristic acid). If we replace $\frac{1}{2}\log 2n$ by $\log n$, the value increases to 7·60. This change alone would lower T by 18°. Thus association has by no means an insignificant effect on the melting points of homologous series.

If our assumptions be correct, the amide will differ from the acid only in the value of the equilibrium constants of the chemically associated groups $(-CO{\cdot}NH_2)_2$ and $(-CO_2H)_2$. The equilibrium constants for these groups are given by $\kappa_3 = (k_3''/k_3')e^{+2Q_3/RT}$, where Q_3 is the heat of crystallisation of the terminal group. Q_3 for the amide is 2·18 Cal. greater than for the acid, and this difference will affect κ_3 very materially and through it the melting point; k_3''/k_3' may be different for the two substances, but the values of this ratio are unknown.

It is clear, however, that the main factor which is responsible for the amide melting 50° higher than the acid is the high heat of crystallisation of the $(-CO{\cdot}NH_2)_2$ group. In (4A), if we assume that the terms in the brackets are the same for the amide and the acid, then Q/T = constant. Q/T for the amide is 0·03436, and for the acid 0·03287, and these values are sufficiently in agreement to warrant the above conclusion.

Non-alternating Series.—The ethyl ester possesses one more point of attachment in the crystal than the methyl ester. This is due to the additional methylene group in the alkyl chain. The equilibrium constant for this group, κ_4, is equal to $(k_4''/k_4')e^{+Q_4/RT}$, where Q_4 is its heat of crystallisation. $Q_4 = 0{\cdot}54$ instead of the normal value 1·03 Cal. found for the acid chain. The equilibrium constant, κ_4, is lower than κ_1 for the groups of the acid chain, or, in other words, the tendency for the methylene group in the alkyl chain to enter the solid state is much lower than for the same group in the acid chain. Thus the low melting point of the ethyl esters, when compared with the methyl esters, can be ascribed to the low heat of crystallisation of the methylene group in the alkyl chain.

Experimental.

The esters of myristic acid and myristyl alcohol were obtained from Eastman Kodak Co., and were purified by distillation or crystallisation until a constant setting point was obtained. Myristamide was prepared from a pure specimen of myristic acid and purified by crystallisation.

The details of the experimental technique were as described previously. The calorimeter had a water equivalent of 345·3 cal./deg.

The experimental data are recorded in Tables II—V. The heats of crystallisation of myristamide and myristyl alcohol are probably correct to within 0·5% and those of the esters to within 1%.

Table II.

Myristamide: setting point, 103·5°.

(Weight of substance, 6·5294 g.; glass, 3·8847 g.; platinum, 0·2008 g.; nickel, 3·3121 g.)

Expt. No.	Temp. range.	Fall in temp.	Rise in temp.	Expt. No.	Temp. range.	Fall in temp.	Rise in temp.
1— 4	64—15°	50·73°	0·586°	11—12	110—15°	95·75°	2·273°
5— 7	100—15	84·75	1·045	13—14	127—15	112·68	2·545
8—10	110—15	95·56	2·278	14—17	139—15	123·94	2·725

I. From 1—7, σ_S = 0·535 cal./deg.
II. From I and 8—17, σ_L = 0·640 cal./deg.; Q = 56·84 cals./g.

A large number of measurements were made over the temperature range 110—139° in order to make quite sure that the high value for σ_L given above was correct. The amide when fused had a pale yellow colour which could not be removed by repeated crystallisation.

Table III.

Myristyl alcohol: setting point, 37·7°.

(Weight of substance, 10·9602 g.; glass, 6·1894 g.; platinum, 0·2008 g.; nickel, 3·9133 g.)

Expt. No.	Temp. range.	Fall in temp.	Rise in temp.	Expt. No.	Temp. range.	Fall in temp.	Rise in temp.
1—3	1—18°	−17·13°	−0·297°	9	34—18°	+15·97°	+0·333°
4	24—18	+ 6·36	+0·119	10—12	39—18	21·23	2·146
5	26—18	8·31	0·156	13	56—18	37·48	2·538
6	28—18	10·09	0·194	14—15	60—18	42·43	2·643
7	30—18	12·08	0·233	16—18	66—18	47·73	2·785
8	32—18	14·01	0·279	19	75—18	57·35	3·032

I. From 1—9, σ_S = 0·432 cal./deg.
II. From I and 10—19, σ_L = 0·612 cal./deg.; Q = 54·86 cal./g.

Myristyl alcohol occurs in two solid modifications, one of which is unstable between 0° and 34°. The above value of Q refers to the modification stable at room temperature.

TABLE IV.

Methyl myristate: setting point, 18·35°.

(Weight of substance, 10·9144 g.; glass, 6·1791 g.; platinum, 0·2008 g.; nickel, 3·0904 g.)

Expt. No.	Temp. range.	Fall in temp.	Rise in temp.	Expt. No.	Temp. range.	Fall in temp.	Rise in temp.
1—3	1—13°	−12·25°	−0·232°	6— 8	20—13°	6·96°	1·526°
4	3—13	− 9·92	−0·190	9—11	50—13	36·93	2·155
5	6—13	− 6·95	−0·135				

I. From 1—5, $\sigma_S = 0{\cdot}475$ cal./deg.
II. From I and 6—11, $\sigma_L = 0{\cdot}526$ cal./deg.; $Q = 43{\cdot}90$ cal./g.

In experiments 6—11, the ester took 60 minutes before crystallisation was complete, as compared with 20—25 minutes for the amide and alcohol. On account of the long middle period, a radiation correction of approx. 0·04° was sometimes applied. This makes the above value of Q less accurate than those of the amide and the alcohol, but the error is not greater than 1%.

TABLE V.

Ethyl myristate: setting point, 11·0°.

[Weight of substance, 11·0523 g.; glass, 4·6576 g.; platinum 0·2008 g.; nickel (except Expts. 6—8), 2·034 g.; nickel (Expts. 6—8), 2·1498 g.]

Expt. No.	Temp. range.	Fall in temp.	Rise in temp.	Expt. No.	Temp. range.	Fall in temp.	Rise in temp.
1	0—15°	−14·58°	−1·678°	6— 8	45—15°	30·09°	0·579°
2	3—15	−11·99	−1·619	9—11	−9—15	−23·99	−1·842
3—5	6—15	−9·32	−1·500				

I. From 6—8, $\sigma_L = 0{\cdot}500$ cal./deg.
II. From I, 1—5, and 9—11, $\sigma_S = 0{\cdot}498$ cal./deg.; $Q = 43{\cdot}6$ cal./g.

Sixty minutes elapsed before the melting of the ester was complete.

Summary.

The heats of crystallisation of a number of derivatives of myristic acid have been determined, and the results have been employed in the calculation of the melting points of certain homologous series, *viz.*, the amides, methyl and ethyl esters of the monobasic fatty acids, and the monohydric alcohols. The calculated melting points are in good agreement with the experimental values.

The effect of the chemical constitution of the polar terminal group on the melting point has been discussed from the standpoint of the theory of melting points put forward previously. The heat of crystallisation of the terminal group is shown to play a dominant part in determining the *equilibrium constant* of the group and, through it, the melting point.

THE RAMSAY LABORATORIES OF PHYSICAL AND INORGANIC CHEMISTRY,
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FARADAY LECTURE

(Delivered before the Fellows of the Chemical Society in the Theatre of the Royal Institution on May 18th, 1927.)

Problems and Methods in Enzyme Research.

By RICHARD WILLSTÄTTER.

NEARLY sixty years have elapsed since the death of Faraday. I count it a unique distinction that I may to-day address the Chemical Society in memory of this great pioneer, in the room so closely associated with his labours. I am conscious that it is a special honour to be allowed to join that small band of scientists from various lands—there have so far been twelve—who have spoken in remembrance of Faraday. In these memorial lectures the history of science is reflected, which, in the image of Goethe, may be compared to a great fugue in which the voices of the nations are heard in succession. My reverence for the genius to whom we pay homage is coupled with veneration for the memory of the many other great investigators whom your country has produced. The presence of so many distinguished colleagues in this room augments my sense of the importance of the present occasion, but my thoughts nevertheless travel beyond the living, to the immortals.

My predecessors have mostly selected single chapters of Faraday's lifework as a starting point for a discourse on experimental contributions or theoretical discussions in the realms of physics and chemistry. Faraday's work provides a store of stimulating suggestions, one which is neither exhausted nor likely to become so for a long time to come. Since none of my predecessors has referred to Faraday's experiments "on the power of metals and other solids to induce combination of gaseous bodies," I should like to take this early fundamental investigation on catalysis as my starting point in a discussion of organic catalysts.

This investigation was carried out in the year 1833, at the time, therefore, of E. Mitscherlich's work on the formation of ether from alcohol by contact with sulphuric acid. Faraday and Mitscherlich recognised the frequency of such reactions. Mitscherlich called them reactions through contact, and compared ether formation to the decomposition of hydrogen peroxide, the alcoholic fermentation of sugars, the formation of acetic acid from alcohol, and the decomposition of urea ("Für sich erleiden diese Substanzen keine Veränderung, aber durch den Zusatz einer sehr geringen Menge Ferment, welches dabei die Kontaktsubstanz ist, und bei einer bestimmten Temperatur, findet diese sogleich statt." . . . By themselves these

substances do not undergo any change, but they decompose at once at a given temperature on addition of a very small quantity of a ferment which is the contact substance).

These investigations were discussed by Berzelius in his 15th annual report on the progress of the physical sciences. He collected a number of known cases of inorganic and organic contact actions, and grouped them for the first time under the definition of "Catalysis." Although he saw in catalysis "a new force causing chemical action, present both in organised and in unorganised nature," he was far from rejecting the idea "that it should be considered an action independent of the electro-chemical relationships of matter."

The inorganic contact substances had, in connexion with the earliest observations on catalysis, already been compared with natural ferments, and when, towards the end of the century, W. Ostwald gave new life to research by his definition of catalysis, his suggestion of kinetic measurements led to the stimulation of enzyme research by the methods of physical chemistry. The parallelism between enzymes and artificial inorganic catalysts was particularly emphasised by G. Bredig through his experiments with inorganic ferments, which revealed a manifold and far-reaching agreement between the two kinds of catalysts. Conversely, observations on the behaviour and the nature of enzymes promise new knowledge of the general theory of catalysis. My own experiments and those of my pupils, of which it is my privilege to speak to-day, deal with the adsorption relationships and some other properties of enzymes, more particularly their specificity. With the great example of Faraday before me, I venture to bring forward these modest contributions, encouraged by the deep interest which Faraday evinced in the nature of the relationship between catalyst and substrate. The expectation does not appear altogether unjustified that some new results with enzymes, pointing as they do to a close relationship between the phenomena of adsorption determined by affinity and those of catalytic action, may contribute to a more general knowledge of the selective action of chemical adsorption and of the specificity of catalysts. In their strict specificity, and also in their great potency within a narrow range of reaction conditions, the enzymes are superior to the long-known inorganic contact substances. The modern development of catalysis in chemical industry has emphasised the importance of the problem of improving inorganic catalysts on the pattern of the enzymes so as to make them more selective and at the same time more active. Moreover the activation of enzymes is being imitated with much success. These phenomena of activation and also those of catalyst poisoning, being susceptible of quantitative measurement, have of late led to

remarkable information concerning the nature of catalysts, for example, in the researches of C. N. Hinshelwood, W. G. Palmer, F. H. Constable, and H. S. Taylor.

Faraday examined the action of platinum on a mixture of hydrogen and oxygen. He rejected the idea that a contact substance enters into a chemical union. It is, however, not quite correct, as has often been done, to quote his explanation of the process as being a purely physical one. Faraday spoke of " that attractive force, possessed by many bodies in an eminent degree, and probably belonging to all, by which they are drawn into association more or less close, without at the same time undergoing chemical combination . . . and which occasionally leads, under very favourable circumstances . . . to the combination of bodies simultaneously subjected to this attraction. I am prepared myself to admit . . . both with respect to the attraction of aggregation and of chemical affinity, that the sphere of action of particles extends beyond those other particles with which they are immediately and evidently in union, and in many cases produces effects rising into considerable importance."

In Faraday's view, catalysis and adsorption are related. As unequivocal examples show nowadays, many adsorption phenomena depend on chemical affinity and more especially on the residual affinity of the molecules. The attempt to explain adsorption by means of capillarity breaks down in the case of selective adsorption, as observations on the selective behaviour of adsorbents towards enzymes show.

The behaviour of hydrogen and oxygen towards platinum has ever remained an important problem since the above-mentioned fundamental investigation by Faraday. As I was able to show a few years ago, in conjunction with E. Waldschmidt-Leitz, platinum is capable of transferring hydrogen catalytically only in the continued presence of oxygen. There are various views with regard to this rôle of oxygen in hydrogenation catalysis. Whilst, on the one hand, M. Bodenstein considers the oxygen merely of importance for the renovation, that is, the detoxication, of the platinum surface, R. Kuhn, on the other hand, has developed the view that the oxygen poisons the platinum to some extent, and that without its co-operation only recombined hydrogen molecules would encounter the substrate on the platinum surface. This view makes the oxygen content responsible for the variety of the recombination stages of the hydrogen at the platinum surface. It should, however, be borne in mind that even the course of the reaction in hydrogenation, for instance of naphthalene (according to R. Willstätter and F. Seitz), may vary according to the extent to which the platinum is charged with oxygen. I consider it, therefore, more probable that the

affinity fields of the platinum are so changed by the taking up of oxygen that a new contact substance results, specifically adapted to the hydrogenation. The greater or smaller extent of the oxygen charge would then produce definite peculiarities in the affinity. Platinum charged with oxygen must be ranged among the mixed catalysts, and may be compared with the enzyme–activator complexes. To my mind the experiments indicate that, according to the nature of the contact substance, the naphthalene is variously activated and thereupon hydrogenated to the different stages that are observed. The existence of some relationship between the contact substance and the naphthalene may be inferred from the fact that with platinum *cis*-decahydronaphthalene is exclusively produced; with nickel, on the other hand, the *trans*-isomeride is the chief product of the hydrogenation.

Berzelius relinquished any attempt to explain the processes of catalysis, and emphasised in his discussions with Liebig the danger of explaining incompletely understood phenomena by means of hypothetical assumptions. To-day this reserve is still maintained and approved by many; the absence of an explanation, however, has limited the interest in the phenomena. There is no single method of scientific investigation which can be described as the right one in all circumstances. A hypothesis may vary in value according to the mentality and the temperament of the investigator and according to its utility in suggesting and co-ordinating new observations. A hypothetical explanation of incompletely understood phenomena is often a necessary condition of scientific progress.

An elaboration of an incomplete attempt at explanation by Liebig may perhaps be seen in the hypothesis of C. Nägeli (1879), who explained ferment reactions by the transference to the substrates of "states of motion," that is, of "vibrations of the atoms and particularly of atomic groups." His view seems to me to have been improved by J. Böeseken and to have been further developed, in accordance with modern conceptions, by the consideration of electron orbits instead of atomic vibrations.

The definition of W. Ostwald (1894), which gave a fresh stimulus to research, is as follows: "Katalyse ist die Beschleunigung eines langsam verlaufenden chemischen Vorgangs durch die Gegenwart eines fremden Stoffes" (Catalysis is the acceleration of a slow chemical process brought about by the presence of a foreign substance). Ostwald considered the principle that the catalyst changes the reaction velocity only, to be the key to the interpretation of catalytic phenomena. As he himself stated, the new point of view which was of most value to research was the conception that a catalyst or enzyme cannot bring about a reaction which does not

occur without its co-operation. This conception still holds the field, although it is true that several investigators (J. J. Thomson, H. E. Armstrong) did not agree with it. This principle, which has been deduced from thermodynamical considerations, should not, however, be maintained too dogmatically. At the present day it seems to me to have little value and to hamper progress. Like a dogma, it hinders us in any attempt to find a new explanation of the phenomena of catalysis without intermediate compounds and of the causation of reaction without an influx of energy.

The catalyst may function in degrees of association with the substrate, varying from *fixation* to *approach*. It can, naturally without extraneous energy, bring about a change of constitution in the substrate molecule, and it is only through this constitutional change that reaction may be induced. Here it is not an essential, nor even a general condition, that the molecule should change to a new compound capable of independent existence, as, for instance, to an isomeride such as the so-called γ-glucose (with a changed oxygen bridge) which has been postulated as an intermediate in the action of F. G. Banting and C. H. Best's insulin on glucose. In general the catalyst only requires to bring about a change in the molecule such as was first suggested intuitively by F. Raschig (1906), in advance of exact interpretation. F. Haber (1922) considers the heterogeneous catalysis of gas reactions to be a process "in which the first phase . . . is apparently represented by an electrodynamic distortion of the molecules by the atomic fields at the interface between the solid contact substance and the gas." M. Bodenstein also bases an explanation of the activation of hydrogen by platinum on the deformation of the molecules.

Our new views concerning the structure of atoms and molecules permit us to characterise the hypothesis of the deformation of molecules somewhat more fully as the deformation of their electron orbits. Making ourselves more independent of the hypothetical formulation of discrete orbits, we may, in accordance with E. Schrödinger's wave mechanics, conceive the action of the catalyst on the substrate, through fixation or approach, to be such that the continuous distributions of the electrical charges of the catalyst and the substrate mutually influence each other. A superposition of the fields of charge associated with catalyst and substrate may amount to the same thing as the presence of points of greater condensation of the charge.

The immense store of facts comprehended in "catalysis" contains examples of so diverse a nature that it would be futile to attempt to explain all the phenomena by means of a single hypothesis. The Ostwald school has proved the existence of intermediate reactions

in important cases. The explanation is derived from A. de la Rive's assumption (1846) of a platinum–oxygen compound and from the much older investigation by N. Clément and Ch. B. Désormes of the action of oxides of nitrogen on sulphurous acid. In the case of homogeneous systems this explanation has proved so fruitful that E. Abel declared : " nicht Stoffe, nur Reaktionen katalysieren " (Only reactions may catalyse, substances do not). It is a weakness in Böeseken's views that they do not contemplate this kind of catalytic reaction. Although many catalytic phenomena may be explained without postulating the formation of stoicheiometrically constituted intermediate products, and although a theory of affinity modification without the production of intermediate stable compounds has its uses, such a theory can nevertheless not lay claim to universal validity. In enzyme chemistry there is no theory which appears to be so fruitful and so satisfactory as that assuming the existence of intermediate compounds between catalyst and substrate. Accordingly this is the specifically chemical conception of the primary process of enzyme action, in contradistinction to the physical one, the colloidal–chemical adsorption process suggested by W. M. Bayliss, G. S. Hedin, and J. M. Nelson.

According to Böeseken a catalyst produces a very rapid change (" dislocation ") of the links which it activates by means of a " temporary, very unstable addition to the specific links of the molecules " (" action orientatrice "), and then, without forming a true compound, transfers peculiarities of its own " open system " by induction to the closed system of the substrate (" action dislocante "). By way of explanation it is represented that the catalyst changes the electron orbits of the substrate. According to N. Bohr's view this deformation of an electron orbit would occur through the action of a force, and would therefore involve a change in the energy of the electron. The assumption of an energy change might be avoided in the case of the superposition of two continuous fields of charge. Thus no change in the energy level or in the distributions of charges would occur.

One of the most general questions on the subject of catalysis is concerned with the chemical nature of the catalysts. The point has hitherto been somewhat neglected, but the above-mentioned observation on hydrogenation catalysis by platinum suggests that our knowledge of the chemical composition, even of simple inorganic catalysts, is still very incomplete. There are many non-specific catalytic actions, especially cases of hydrolysis which are catalysed by acids and alkalis. Thus the non-specific catalytic activity of hydrogen ions may bring about the fission of proteins and their degradation products, of carbohydrates, whether composed of many

or only a few monose-units, and of the fats and other esters. The need for selective and highly active inorganic catalysts has in the last seventeen years led to remarkable results in directing the course of reactions by means of mixed catalysts. These results, possessing great practical value as well as theoretical interest, are largely due to the investigations of A. Mittasch and others in the laboratory of the Badische Anilin- und Soda-Fabrik.

A fundamental conclusion reached by Mittasch is "that the catalytic action of iron becomes both more intense and more permanent on the admixture of numerous metals and oxides." In the catalytic oxidation of ammonia, ferric oxide to which bismuth oxide has been added gives, according to Mittasch, quite as good results as an efficient platinum catalyst. Yet another example among many: pure zinc oxide acts on a mixture of carbon monoxide and hydrogen under pressure in the direction of methanol formation; if a small quantity of iron is added, the reaction is diverted towards the formation of hydrocarbons. The oxidation of carbon monoxide by means of air at the ordinary temperature was made possible by the use of certain mixtures of the oxides of the heavy metals, for example, those of manganese, copper, cobalt, and silver (hopcalite), in the experiments of A. B. Lamb, W. C. Bray, and J. W. C. Frazer. These mixed catalysts have close analogues among the enzyme systems; trypsin differs from trypsinkinase, and papain from papain–hydrogen cyanide, not only in potency, but also in specificity.

It is not enough to assume that the admixture to the simple catalysts merely increases the frequency with which the catalytically active atoms project from the lattice. This effect is produced by only a small category of added substances, the carriers. It is rather that catalysts composed of two or more substances are so clearly characterised by specific actions, or deflection of the reaction, that the status of new substances must be ascribed to them. Hitherto it has been generally accepted as a principle in chemistry that the chemical properties of the constituents are lost in compounds, but are preserved in mixtures. This principle has ceased to be valid since more delicate chemical means have become available for the detection and measurement of chemical affinities. Observations on platinum containing oxygen, on the activated catalysts or mixed catalysts of Mittasch and his co-workers, as well as on activated enzymes, have convinced me of the validity of the statement that *mixtures may have the nature of new chemical compounds*. The similarity between mixtures and compounds may be explained by considering that the electrostatic and the electromagnetic fields of force of the individual components of an intimate

mixture may exert a mutual influence on each other. Thus a new kind of affinity field would result. The same explanation as that already brought forward for the action of a catalyst on the substrate, be it a deformation of electron orbits or a superposition of fields of charge, may be adduced. Thus it becomes intelligible that, by mixing two or more components, individual catalysts may result having an enzyme-like specificity and potency comparable with that of homogeneous compounds; whereas the comparatively simply constituted fields of affinity of the elementary atoms do not suffice for this purpose. The very narrowest range of specificity is a peculiar property of the organic catalysts of high molecular weight produced by the living cell. There appears to be a deep gulf between the inorganic catalysts and the enzymes, the chemical constitution of which is still quite obscure. In reality this gulf has already been bridged by accurately defined organic compounds which act like enzymes.

Chlorophyll may be considered one of the organic catalysts; I have refrained from calling it an enzyme, as this would have been a mere empty phrase. It is now, however, becoming useful to recognise connecting links between enzymes on the one hand and catalysts, accurately defined chemically, on the other. Colloidal chlorophyll forms a dissociating additive complex with carbon dioxide. In conjunction with A. Stoll I have suggested as an explanation of photosynthesis that the adsorbed radiation produces a molecular rearrangement of the carbon dioxide. An isomeric peroxide form of the latter would then decompose into oxygen and hydrated carbon.

Similarly oxyhæmoglobin partakes of the nature of enzymes. Recently I have shown, in conjunction with A. Pollinger, that the oxyhæmoglobins of various animal species act exactly like peroxydases of an unequal potency. Under similar conditions 1 mg. of the oxyhæmoglobin from horse blood, ox blood, and pig's blood furnishes respectively 0·152, 0·114, and 0·093 mg. of purpurogallin in the oxidation of pyrogallol. The oxyhæmoglobins do indeed correspond to peroxidative enzymes of low potency, as they are about 10,000—30,000 times weaker than our best preparations of vegetable peroxydases. We attribute the difference in potency of the individual hæmoglobins to the fact that the same specifically active (prosthetic) group is influenced in its action by association with the globin molecules, which in the various varieties of blood differ in their constitution. The peroxidative reaction of the iron-containing pigment group which is united to various globin complexes is therefore subject to modification, so that the hydrogen peroxide adsorbed by the individual oxyhæmoglobins is activated in a varying degree.

Hence differences in the constitution of the colloidal carrier of the active group result in differences in the potency of this group. This may show how the differentiation of the enzymes, the so-called species specificity, may be determined by variations in the colloidal complex.

The dependence of catalytic activity on chemical constitution has recently been further investigated in the Munich laboratory by R. Kuhn and L. Brann in quantitative experiments with hæmochrome; they used as examples enzyme-like catalysts with accurately defined differences in their chemical constitution. If hæmoglobin is broken down to hæmin, the peroxydase action is enfeebled and the new form of organically bound iron shows a considerable catalase activity which was previously lacking. According to a letter from Prof. R. Kuhn, the activity of hæmin, functioning as catalase, may, under the best conditions, be related to that of G. Bredig's colloidal platinum as 1 : 1·5, and to that of the best preparations of liver catalase, purified by S. Hennichs's adsorption process, as 1 : 1000. In mesohæmin, which is richer by two atoms of hydrogen, the dependence on the p_H of the peroxidative action is considerably changed (optimum 6·5, instead of 5) and the catalase action is lacking. We see, therefore, that the catalytic action is subject to considerable variation without change in the iron content and without the possibility of attributing the variation to changes in the degree of dispersion.

Gradations in colloidal dispersion cannot provide an explanation of the highly selective and specific affinities of enzymes. A few years ago it still seemed doubtful whether enzymic actions depend on peculiar conditions in the dispersion of any known substances, or whether they depend on definite organic compounds of unknown constitution. Our views on this fundamental question have been clarified more especially by the three following sets of observations:

(1) In some cases chemical analysis had caused enzyme action to be ascribed to known organic substances or types. The enzymes which had served for the analyses were, however, very impure; they contained only a few units per cent. or even a fraction of a unit per cent. of the purified enzymes available to-day. According to A. Fodor, the saccharase of yeast was supposed to be substantially identical with a carbohydrate yeast-gum, but now the enzyme has been wholly freed from yeast-gum without change of activity. More frequently and with more reason relationships have been assumed between enzymes and proteins. Thus E. Fischer, in his Faraday lecture, deduced from observations then available, indeed with a certain degree of probability, that the enzymes "are derived from proteins and possess a protein-like character." In a variety of cases it has, however, been possible to purify enzymes to

such an extent that the protein reactions disappear completely (lipase, peroxydase, saccharase).

(2) It results from recent observations by H. Kraut and myself that simple inorganic colloids, showing peculiarities which were likewise thought to be attributable to dispersion, actually owe their specific properties to the individual chemical structure of their molecules. The gels of alumina, ferric oxide, stannic acid, etc., do not consist of metallic oxides with various quantities of adsorbed water, but there are numerous metallic hydroxides with various amounts of water in chemical combination.

(3) In making pure preparations of enzymes from the living cell, they are subjected to great changes in dispersion in the passage from the cells into solution, then into adsorbates, and again into solution; mixtures of enzymes could be separated into their components. Yet in many such cases the enzymic action was preserved almost quantitatively.

The conception of the enzymes as peculiar organic compounds suggests the problem of isolating them in a state of purity. The task of increasing the concentration of the enzymes has progressed so far that they may be more accurately characterised. For we can now distinguish between the properties of the enzymes themselves and the influence of accompanying substances, some of which form with the enzymes naturally occurring, physiological complexes, whilst others become accidentally associated with them during the isolation from the cells. In order to increase the concentrations of the enzymes, which are very low *in situ* or in the crude extracts, it is essential to measure each step in the isolation and purification so far as may be possible by quantitative estimations of the relative activities of the preparations. The literature of the simplest inorganic contact substances seems as yet to be poor in such observations. When, for instance, a metallic catalyst is obtained by reduction of its oxide, it is customary to be satisfied with the conversion of an unknown small fraction of the atoms of the crystal structure into the condition in which they are available for catalysis; that is, into a condition of high energy, of smallest saturation by the other atoms of the crystal lattice. The ratio between the catalytically active atoms and the total number in the case of iron catalysts was determined last year by J. A. Almquist in experiments on poisoning by oxygen. The preparation of an inorganic catalyst should aim at increasing the efficiency of unit weight as far as possible. In the isolation of an enzyme we aim at diminishing as far as possible the mass of catalyst necessary for a given action under definite conditions.

The very labile and very soluble enzymes must be separated from

many times their weight of accompanying substances such as proteins, carbohydrates, and salts, to which they are apparently united by adsorption, and this separation must be effected without the use of the ordinary chemical means, such as conversion into salts or other derivatives. The general method which has been adopted in the investigations of recent years consists in the application of the processes of adsorption by so-called surface-active substances, such as alumina, kaolin, lead phosphate, tristearin, etc. Adsorption is made so selective that not only are the enzymes largely freed from foreign admixtures, but many are also separated from the accessory substances or activators, with which they form complexes.

The application of adsorption processes to the purification of enzymes goes back far into the past. It does not, however, seem to have been well known, or it has been considered doubtful or improbable, that the enzyme could actually be freed from the adsorbates by a process of elution. The small amount of active affinity by which the enzymes are bound in the adsorbates may in general be overcome by very gentle chemical means, for example, by very dilute solutions of alkalis or alkaline phosphates. In this case we do indeed often observe, for instance with lipase, that the elution of an enzyme which takes place quite easily and in good yield in the early adsorption processes becomes more and more difficult as purification proceeds, giving smaller and smaller yields until finally these means fail to decompose the adsorbates. At lower degrees of purity the adsorbents generally also bind certain substances which accompany the enzymes as adsorption complexes; these substances are able to co-operate in bringing about elution as well as adsorption, and sometimes this is the only mechanism for effecting these processes (co-adsorbents and co-eluents).

The oldest reference to the adsorption of enzymes which I have been able to find is the isolation of pepsin by A. Vogel (Munich, 1842). Pepsin was precipitated together with proteins by means of lead acetate, and again passed into solution when the precipitate was treated with hydrogen sulphide. One of the oldest references of this kind is the investigation by E. Brücke (1861), who was able to bind pepsin " mechanically to small solid bodies " such as calcium phosphate, sulphur, or cholesterol and to free it again from the adsorbates. Even in those days, particularly in the following year, A. Danilewsky and J. Cohnheim attempted in Kühne's laboratory to separate enzymes, more particularly the components of the pancreatic mixture, by means of adsorption processes. Differentiation of this kind was met with much later by S. G. Hedin, who found that two proteases present in the spleen behaved differently during adsorption by kieselguhr.

The adsorptive method, which had almost fallen into oblivion, was revived some twenty years ago in an investigation of L. Michaelis and M. Ehrenreich. In using adsorbents of such a kind that they have under all conditions a definitely electropositive or electronegative charge, it appeared as if the opposite charge on the enzymes, whether basic or acid in nature, determined their adsorption. Thus saccharase was believed to be an acid and trypsin to be amphoteric. It has been found, however, that these results are not valid for the enzymes themselves, but only for arbitrary aggregates of foreign substances which happen to be present in the impure solutions. Thus saccharase, which was not supposed to be adsorbed by electronegative kaolin, is readily adsorbed by this substance after the first few stages of purification, or even at once from autolysates of yeast prepared by an improved method. In many cases the true adsorption behaviour of an enzyme only appears clearly in the course of its purification. Pancreatic amylase, for example, may be adsorbed by alumina under certain conditions, as long as it is in the crude state. The purification of the enzyme can be effected by preliminary adsorption, that is, by removal of a portion through fractional adsorption, but its behaviour then changes so that it is no longer appreciably adsorbed under any conditions by alumina gels of excellent adsorptive power. The adsorption of enzymes is determined by chemical peculiarities which cannot be predicted.

Whilst amylase escapes adsorption, peroxydase provides a case of an enzyme being adsorbed not, indeed, from aqueous solution, but from one containing alcohol. The acidity of the solution commonly has an influence on the adsorption. Papain is very weakly adsorbed from an acid solution, better from a neutral one, still better from a weakly alkaline one, and in this case also much more readily from a solution containing alcohol; it is eluted from the adsorbent by weak acid. Experiments show that these adsorption processes are not at all governed by the capillarity of the substances whose surfaces are strongly developed, nor is adsorption in any way determined by such gross differences as the acid and basic nature of the enzyme and of the adsorbents. Among the various aluminium hydroxides the meta-compound (AlO_2H), which does not appreciably react either with concentrated hydrochloric acid or with sodium hydroxide, is distinguished by the most selective adsorptive action.

The success of the preparative application depends on whether it is possible to make the adsorption sufficiently selective. The smaller the quantity of adsorbent which is required, the higher is in general the degree of purity in the adsorbate. It was therefore necessary to follow the adsorption by quantitative measurements which determined the number of enzyme units taken up by 1 gram

of an active adsorbent (adsorption value). In our first investigation of saccharase we obtained an adsorption value of 0·15 for alumina by improving the autolysates of yeast, by preparing suitable kinds of alumina, and by the choice of conditions favourable to adsorption. Later this value was increased twelve-hundred fold, to 200, by the proteolytic degradation of substances accompanying the enzymes, by using suitable conditions of dilution and acidity, by repetition and by fractionation. Thus the enzyme from 14 kilos. of fresh brewers' yeast was adsorbed by 1 gram of aluminium oxide and the adsorbate weighed 2·5 grams.

A more accurate insight into the course of adsorption is furnished by the adsorption isotherm according to H. Freundlich, which expresses the relationship between the quantities of enzyme in the adsorbate and in the residual solution. Since in the case under review we are not concerned with homogeneous substances, but with complicated mixtures, the adsorbed quantities depend very greatly on the initial concentrations. In the case of saccharase the use of very dilute solutions brings about a great improvement in the selective action and in the purity of preparations. Adsorption curves also show in which direction in a given case fractionation should be applied, whether the degree of purity will be improved by removal of the first or of the last fraction. Thus fractionations were controlled by the quantitative studies of H. Kraut on the adsorption behaviour of mixtures. The object was to obtain normal adsorption isotherms such as are given by homogeneous substances, and this has been attained in the case of certain enzyme preparations (saccharase). Once this is attained, the same adsorption process does not, of course, bring about any further improvement. Yet the preparations so obtained were found to be far from homogeneous. The observed adsorption curves are not those of the enzymes themselves, but of enzyme-containing complexes. The adsorption method reaches a limit of utility with certain aggregates in which the enzymes and substances most nearly related to them are firmly joined by adsorption to accompanying substances of different kinds. The proof that the constantly adsorbed enzymes are only apparently single substances follows from qualitative and quantitative analysis. If a given constituent can be tested for by colour reactions or by precipitation, it must be possible either to accumulate it or to get rid of it completely. For instance, my first investigation (with A. Stoll) on vegetable peroxydase led to preparations of which sugar groups formed a considerable part. They showed an important iron content (0·5%) which seemed to be approximately proportional to the peroxidative action. Starting from this condition, the degree of purity could be raised about

fivefold by adsorption methods : meanwhile the carbohydrate constituents were eliminated and the iron content fell to one-seventh (0·06%). Hence iron does not enter into the constitution of this oxidative ferment. At the degree of purity ultimately attained, a new property of the enzyme appeared, which could not be recognised at an earlier stage : the enzyme had a reddish-brown colour resembling that of porphyrins.

Phosphorus seemed to be an essential constituent of saccharase, for its quantity amounted to 0·16—0·19% for saccharase of saccharase value 0·1—0·15 (H. von Euler and O. Svanberg). A fractionation was then carried out by means of adsorption on lead precipitates in such a way that the enzyme was isolated from the fractions containing least phosphorus. While the saccharase value rose to 2 and further to 5, the phosphorus content fell to 0·02 and even to 0·006%. The change in the ratio phosphorus : activity shows that this constituent is of no significance.

There is no sure method available for freeing the enzymes from the protein derivatives. However, if a certain enzyme in isolated cases could be freed quantitatively from accompanying proteins, this might be considered a sufficient demonstration that this enzyme neither is a protein nor requires protein for its activity. Nevertheless the tenacity with which proteins cling to enzymes has threatened again and again to impose the conclusion that the enzymes are of a protein character. Progress in the technique of methods of separation has been achieved mainly with yeast saccharase. Autolysates of yeast and the enzyme preparations made from them always gave the strong Millon reaction of tyrosine peptides, about as strongly as egg albumin. But the protein fission products responsible for this reaction only accompany the enzymes in the course of the proteolytic degradation to which the yeast plasma is subjected after destruction of the cell. It was therefore only necessary to carry out a cautious autolysis of the yeast at neutrality and to avoid the proteolytic processes in the isolation of the enzyme, in order to free saccharase completely from the substance giving the Millon reaction. On the other hand, the enzyme preparations which have been obtained in this gentle fashion are characterised by a striking tryptophan content which was discovered by H. von Euler and K. Josephson, who attributed to it a real importance as regards the composition and the function of saccharase. Actually it has been found impossible to free saccharase entirely from tryptophan by any systematic process of adsorption, but it was nevertheless possible in single cases. And my purest preparations of this enzyme show only about $\frac{1}{4}$ to $\frac{1}{8}$ of the tryptophan content found in the preceding research (saccharase values 8·4, 11·9, and 9·7 with 0·12, 0·16, and

0·18 mg. of tryptophan per unit). The crude material, the autolysate of yeast, can, however, be obtained in such a way that after dialysis it contains much less of this amino-acid than was considered to be characteristic of the pure enzyme. The quantity of tryptophan for different saccharase units is 150 mg. in the case of ordinary yeast and 70 mg. in the autolysates formerly employed. By increasing the enzyme content of the yeast itself and by improvements in the autolysis, the quantity of tryptophan corresponding to one unit was lowered to 0·23 mg. in the case of an autolysate after prolonged dialysis. Saccharase could therefore be freed almost completely from various chemically recognisable substances of rather high molecular weight, such as carbohydrates, phosphorus compounds, and protein substances, and this without loss of activity, even without loss of stability.

By the adsorption processes the saccharase is concentrated 3000—4000 fold as compared with dry brewers' yeast. The enzymic concentration of the purest preparations corresponds to saccharase values of 11—12 obtained from the yeast autolysates of a saccharase value equal to $\frac{1}{150}$. After this degree of purification had been reached, it seemed desirable to increase the purity of the yeast itself and of its autolysates, and to test whether a greater increase of the enzymic concentration could thereby be achieved. It is possible to make yeast richer in enzymes. H. von Euler and also J. Meisenheimer had increased the saccharase content of yeast considerably by prolonged intensive fermentation. Their results were soon greatly improved upon by conducting the fermentation with very low concentrations of sugar so that the saccharase content was increased ten to fifteen times, while other enzymes, such as maltase, trypsin, and the members of the zymase complexes, suffered only a slight increase or none at all. The importance of this process therefore consists in increasing the ratio of the saccharase to those other enzymes from which it may be separated only with the greatest difficulty. Improvements were also made in the method of dissolving the enzyme, and in this connexion it was necessary to reach a better understanding of the processes which take place on the passage of an enzyme from the yeast cell into aqueous solution. The cell begins to give enzyme to the water only after its death. The liberation of a sucroclastic enzyme is itself an enzymic process and indeed a definite stage in the entire enzymic degradation of protoplasm. The liberation of the saccharase and of the maltase must therefore be separated as far as feasible from the whole process of yeast autolysis. It was possible to make these two enzymes pass quantitatively into aqueous solution in the course of a single day, accompanied by not more than one-tenth or even only one-twentieth

of the substance of the yeast. The crude solutions attain saccharase values of about 1, and the dialysed solutions values of about 2·5; whereas a few years ago the purest known preparations corresponded approximately to the value 0·3. By means of the adsorption method the autolysates, obtained with the greatest possible precaution, now readily yield the enzyme, but not in a greater state of purity than the earlier autolysates, which were 100—375 times weaker. The enzymic concentrations are on the whole even a little lower, but the stability of the enzyme is greater. Here, indeed, the natural enzyme complexes seem to have been isolated by gentle means. In energetic autolysis, followed by a proteolytic process, the mass of these complexes becomes less and they become less stable. It seems that we must consider an enzyme to be composed of a specifically active group and a colloidal carrier. To this, other substances of high molecular weight cling in various ways. The colloidal carrier seems to vary somewhat in its nature, but to be necessary for the stability of the active group.

In the whole course of enzyme isolation the adsorption method has so far only served to separate the enzymes from substances which are not closely related to them. In every case the components that are most tenaciously retained are those substances which are most closely related to the enzyme in colloidal and chemical properties, for instance, its transformation products, which differ from it only by the absence of the active specific group. In this connexion we attribute importance to a process of fractional adsorption, that is, adsorption on a very finely divided precipitate, for instance, of lead phosphate, produced in the enzyme solution itself. The highest degree of enzymic purity yet attained has been reached by a fractional formation of such an adsorptive precipitate. By this means it has also become possible for the first time to separate an enzyme from the products of its inactivation, when a loss of activity has occurred through keeping or warming a solution; the more easily adsorbable portions contain the inactive, and the more difficultly adsorbable ones the active, fraction of the enzyme.

The most important and theoretically interesting problems of the adsorption method are presented by (1) the complexes of enzymes with their activators and their retarders, and (2) the natural mixtures of enzymes.

The pancreatic mixture of lipase, trypsin, and amylase offers the first example of the separation of enzymes by means of adsorption. Lipase is most readily adsorbed; it can be removed from the mixture by means of alumina and eluted from the adsorbate by means of weakly alkaline phosphate solution. Amylase and trypsin remain in solution. It should be borne in mind, however, that this

process requires the use of a particular kind of alumina (γ-alumina). Another kind (β-alumina) readily adsorbs the trypsin as well. Pancreatic amylase is the least adsorbable, in a pure condition scarcely at all by ordinary means. For solutions which are still impure, kaolin is suitable for the complete adsorption of trypsin, leaving amylase behind. This investigation was continued by E. Waldschmidt-Leitz in my laboratory, and he succeeded in completely resolving the proteolytic systems of the pancreas and the intestine. In consequence of the detailed experiments of W. M. Bayliss and E. H. Starling, trypsin was supposed to be secreted by the gland in the form of an inactive precursor (trypsinogen) and changed into trypsin itself by a second enzyme, enterokinase, which accompanies it. Enterokinase is, however, no enzyme, but a specific activator of trypsin. This kinase may be separated from trypsin by adsorption with alumina, even after the latter has been activated. What was considered to be trypsinogen is a true enzyme which even in the absence of its kinase has a specific action on peptones, histones, and certain protamines. Activation by enterokinase increases the activity and extends it to more resistant substances such as fibrin, gelatin, casein, etc. Trypsin and the trypsin–enterokinase complexes prove to be two proteases differing in specificity and complementary to each other. The best means of separating trypsin and enterokinase depends, according to E. Waldschmidt-Leitz and K. Linderström-Lang, on the adsorption of the activator by a precipitate of casein produced in the solution; the trypsin remains behind quantitatively. Since trypsin free from its activator and also enterokinase are both obtainable in a state of purity, the enzyme and the kinase of various animals may be compared and combined. E. Waldschmidt-Leitz found that the trypsin of one species is activated by the kinases of other animals in quite unequal degrees; for instance, the trypsin of the pig is activated much more strongly by the kinase of the cat than by the corresponding kinase of the pig.

Apart from kinase, pancreatic protease consists of two components, the second being erepsin, discovered by O. Cohnheim in the intestinal mucous membrane. Of the two proteolytic enzymes, only erepsin is readily adsorbed by alumina (γ), according to E. Waldschmidt-Leitz. On repetition of the adsorption several times, the separation becomes complete. In the same way we can separate, by means of adsorption on alumina, the two proteases of yeast, but in this case the tryptic component is the more readily adsorbable. It is only when the enzymes of a mixture have been thus prepared in a homogeneous state that it is possible to determine their specificity. Erepsin does not act on the higher proteins, but exclusively

on the simpler peptides—a point which was hitherto doubtful. The homogeneous proteolytic enzymes will in future research be the most suitable agents for the fractional enzymatic hydrolysis of proteins, in order to determine analytically the various stages in their degradation, and for preparative purposes.

Whilst the first-mentioned example was concerned with the three pancreatic enzymes, differing greatly in specificity and in properties, the last-mentioned applications of the method extend to similar closely related enzymes in which only small differences in adsorptive behaviour would be expected. The adsorption could therefore be made sufficiently selective to render possible the separation of enzymes acting on closely related substrates. This property, which cannot be explained at present, is also the only one which makes possible the separation of the enzymes that split sucrose and maltose respectively. The relation between the adsorptive actions of various alumina gels on solutions of a given enzyme, for instance, of saccharase, does not hold equally for any other enzyme, and is, for instance, quite different in the case of maltase. Thus there are varieties of alumina (β- and the meta-hydroxide) which are capable of taking up maltase comparatively readily from yeast autolysates, but saccharase only sparingly. In this way it is possible, even by a single application of the process, to obtain adsorbates, and from them again, by means of secondary alkali phosphate, solutions of enzymatically homogeneous maltase; at the same time the solutions of the saccharase are completely freed from maltase with little loss. The selective adsorption may be replaced by a process of selective elution from the adsorbates. By means of γ-alumina saccharase may be adsorbed together with maltase. Weakly alkaline or neutral phosphate solution then liberates both enzymes from the adsorbates, but a primary phosphate liberates saccharase completely and almost exclusively. The greater part of the maltase remains behind in a homogeneous condition and can be isolated by means of a secondary phosphate.

The adsorption of enzymes and their activators by various adsorbents is due to the qualitatively different affinities of single groups of atoms, and must be conceived to be similar to the action of an enzyme on its substrate. This dissimilar behaviour, utilised, for example, in the separation of saccharase from maltase, may, I believe, be attributed to differences in the chemical constitution of these enzymes and indeed to differences in their specific active groups.

In many cases there are indications as to which atomic groups of an enzyme are responsible for its union to an adsorbent. There are adsorbates of saccharase on alumina which under certain conditions hydrolyse sucrose just as rapidly as the saccharase contained in them

would in free solution. On the other hand, the enzymatic activity of pancreatic lipase is to a large extent destroyed in its adsorbates on tristearin or on cholesterol. This suggests a participation of the specifically active group in the adsorption process. The lipase may be liberated again in an active condition from its almost inactive adsorbates. According to recent observations of E. Waldschmidt-Leitz and K. Linderström-Lang, enterokinase is inactive in the alumina adsorbate; its trypsin-binding group is occupied. On the other hand, the alumina adsorbates of trypsin and of trypsin-kinase are quite active.

The most delicate gradations in adsorptive power are determined by the peculiar chemical differentiation of the gels used, particularly of alumina, and by their preparation in a homogeneous state. Until quite recently the view prevailed that the gels of alumina precipitated from salts consist solely of aluminium oxide with adsorbed water and that their ageing results in a diminution of dispersivity, accompanied by a diminution of their adsorptive power. It is found, however, that the power of adsorbing saccharase increases rather than diminishes with the ageing of an alumina precipitate. The greater age of the gels brings about, not changes in dispersivity, but changes in chemical constitution. Under certain conditions the first aluminium hydroxide (α) may be isolated as an unstable gel of the formula $Al(OH)_3$. It changes in the course of a few hours into a second modification (β) and then very slowly into a third stable gel (γ), likewise of the composition $Al(OH)_3$. By heating it with ammonia to 250° there results yet another gelatinous aluminium hydroxide, the molecule of which contains less water; it corresponds to the formula AlO_2H. The chemical differences between these colloidal precipitates are very great, but there is no simple relationship between their basic and acid properties and their adsorptive powers. Inorganic chemistry will find a large field for the investigation of structure among such gelatinous hydroxides.

One of the results which we owe to the adsorption method is a knowledge of the enzymes in a higher state of purity. Most of the properties which had been ascribed to enzymes depended on their degree of purity and may be simulated, or deceptively altered, by accompanying substances, or at least influenced by them. The behaviour of an enzyme is thus influenced partly by quite foreign substances, accidentally associated with it in the course of the isolation, and partly by companions of physiological importance which co-operate with the enzyme when it occurs naturally. The influence of the accompanying substances extends to the stability of the enzymes, to the temperature of their destruction, to the temperature of their optimal activity, to their behaviour on

adsorption, to their behaviour towards activators, inhibitors, and poisons, and even to the dependence of the reaction velocity on the hydrogen-ion concentration of the solution and on the concentration of the substrate.

With regard to both the control of the quantities of enzyme in preparative work and also a knowledge of the specificity of the enzymes, it is very important to remember that the comparison, by means of the reaction constant, of quantities of various enzyme preparations, of different origin and of different degrees of purity, may not be trustworthy. The relationship between the relative quantities of enzyme and the corresponding velocities may differ in various preparations of one and the same enzyme. And even when this relationship is constant, it is still uncertain whether equal velocities correspond to equal absolute quantities of enzyme in various solutions. In this respect some information is given by the dependence of the reaction velocity on the conditions of experiment. Since the fundamental investigations of S. P. L. Sörensen and of L. Michaelis and P. Rona, the dependence of the reaction velocity on the hydrogen-ion concentration of the enzyme solution has been recognised and taken into account. The measurement is usually carried out at the optimal p_H; a comparison is made between equal fractions (equal percentages) of the reaction velocities, maximal in relation to p_H. But even when there is a correspondence in the dependence on the p_H, the dependence of qualitatively similar enzyme preparations on the concentration of the substrate may still vary greatly as was shown in investigations made by R. Kuhn in my laboratory. At equal concentrations of the substrate, arbitrarily varying fractions of the maximal reaction velocity may be found. This varying dependence on p_S may be caused by inhibitors of the enzyme, accompanying substances which bind the specifically active group of the enzyme. The reaction velocities extrapolated for infinitely great substrate concentration then give a true measure of the quantities of enzyme. For this reason we propose reduced units of mass, for instance, for saccharases of different origin. The comparison of the velocities of fission at corresponding concentrations of the enzyme–substrate compound has made it possible to recognise more clearly the specificity of sugar- and glucoside-splitting ferments. Thus it has been ascertained that the hydrolysis of sucrose and of raffinose must be attributed to the same enzyme, saccharase (according to R. Kuhn); the hydrolysis of maltose and the various α-glucosides to the same maltase; and the hydrolysis of the various β-glucosides to the same β-glucosidase of emulsin. It may also happen that the accompanying substances do not attach themselves to the active group, but to other parts of the enzyme molecule, parts

which are not directly concerned with the binding of the substrate. In many such cases the influence of qualitatively and quantitatively varying companions may be overcome by arbitrary additions, that is, by compensatory activation or by compensatory retardation, so that the quantities of the enzyme may be deduced with sufficient accuracy from the reaction velocities (estimation of the lipases).

The dependence of enzymic activity on p_H and p_S may vary according to the degree of purity of the enzyme. An example of the variability of the p_H optimum is afforded by the lipase of the stomach. In the human stomach, lipase, in contradistinction to pancreatic lipase, has the optimum action in the acid region, at p_H 5—6; the same applies to the stomach of the dog. The activity–p_H curve and the position of the optimum are constant for the unpurified lipase of any species, but this constancy is not a property of the enzyme itself. If this lipase is purified by an adsorption process with kaolin, an accompanying substance, which inhibits in alkaline solution, is removed, and apparently also a substance which activates in acid solution. After purification, human gastric lipase has the optimal activity in alkaline solution at $p_H = 8$.

The only property of the enzymes which is independent of the purity is, as far as we know, their qualitative specificity, their adaptation to a definite set of reactions determined by constitution and configuration. As the history of the proteases shows, this specificity remained indeterminable in certain cases, and was indeed determined incorrectly where the enzymes occurred in a non-homogeneous condition, as, for instance, erepsin together with trypsin, and as long as it was impossible to test them in a homogeneous condition. This specificity relating to chemical structure seems to be confined within narrow limits among the carbohydrates, but seems to be much less pronounced among the lipases and esterases. The lipatic enzymes of the pancreas, the liver, the stomach, etc., are adapted to the hydrolysis of higher and lower glycerides and of higher and lower esters of monohydric alcohols. The observations made hitherto have not necessitated the assumption that these enzymes are mixtures of the lipases proper with esterases. It seems rather that good esterases, such as that of the liver, are at the same time feeble lipases and that, conversely, good lipases, such as that of the pancreas, are esterases of low potency.

The determination of the specificity to chemical structure reveals the greatest degree of differentiation among the carbohydrases. It is even possible to ascertain the particular atomic group of the substrate molecule towards which the enzymic activity is directed. The enzymes which hydrolyse a compound sugar may attack the molecule in various places. This idea of assuming variously con-

stituted intermediate reaction products in the enzymic fissions of the same substrate was first put forward by E. F. Armstrong (1904) in the case of the lactases of bitter almonds and of Kefir yeast. He found that the former is not appreciably inhibited by galactose, but strongly by glucose, whilst the latter is only influenced by galactose. The diversity in the points of attack and in the course of the reaction in the hydrolysis of the same compound sugar by hydrolytic enzymes was decisively shown in the investigations of saccharase by R. Kuhn and H. Münch (1923—26). Some saccharose-splitting enzymes react with the glucose half of this disaccharide (saccharase from *Aspergillus oryzæ:* gluco-saccharase inhibited by α-glucose); there are others, however, which exclusively attack the fructose portion of the molecule (saccharase from the usual laboratory yeasts: fructo-saccharase, inhibited by fructose). This sharp division of the various saccharases from animal organs, from fungi, and from higher plants into gluco- and fructo-saccharases seemed unjustifiable when H. von Euler and K. Josephson found that saccharase from Stockholm bottom yeast is also measurably inhibited by α-glucose. It could be shown, however, that the frequently occurring inhibition by α-glucose has nothing to do with the relation of the saccharase to saccharose, that the saccharase of the investigated yeasts possesses no affinity for α-glucose. The yeast saccharases in question hydrolyse all known gluco-derivatives of sucrose in which the fructose group, which determines the reaction with the enzyme, is intact, for instance, raffinose of the formula galactose<glucose<>fructose. On the other hand, R. Kuhn and G. E. von Grundherr found that melezitose of the formula glucose<fructose<>glucose is not attacked at all by yeast, but is hydrolysed by taka enzyme (gluco-saccharase).

A special case of specificity due to chemical structure is that caused by configuration. According to E. Fischer, this influence seems to be less pronounced among lipatic enzymes than among those that hydrolyse glucosides. The first example of stereochemical selection by a lipase occurs in an investigation by H. D. Dakin (1903—1905), who observed unequal rates of hydrolysis of the enantiomorphs of racemic esters of the mandelic acid group by means of an enzyme from liver. Such a preference for one enantiomorph enables us to distinguish all lipatic enzymes from one another. When I compared the action of a number of esterases, *viz.*, pancreatic, gastric, hepatic lipase, and taka-enzyme, on racemic esters of substituted phenylacetic acids, I found them all different in their selective action. Considering, however, the close association of lipases with activating companions, one is led to suspect that this specificity varies with the degree of purity. Hence this example is especially suitable for testing the question whether accompanying substances

are responsible for the optical specificity or whether the lipases preserve their stereochemical peculiarities after purification. In an unpublished investigation (in conjunction with E. Bamann and J. Waldschmidt-Graser) it was found possible to increase the degree of purity of lipases considerably and to remove the associated substances which influence the reaction velocity. Gastric lipase (of the pig) was concentrated to 800—1000 times the original enzymic concentration, and thus freed completely from mucin-like admixtures. The stereochemical specificity of the purified lipatic enzyme remained, however, and still remains, qualitatively unchanged. It may, therefore, with a somewhat greater degree of probability than heretofore, be attributed to the enzyme itself.

Our views concerning the relations between enzymes or other catalysts and their substrates, between enzymes or other catalysts and their promoters and retarders, between enzymes and their adsorbents, depend on the assumption of affinities which cannot be formulated in the same way as the affinities in the constitutional formulæ and reaction equations of simpler organic compounds. The wide field of molecular affinities is not yet suitable for exact representation, nor has it yet been opened up to it. The lack of a strict formulation should not prevent us, however, from penetrating into this region of molecular forces and from collecting facts concerning the capacity of molecules to unite with one another. In view of the imperfection of our explanations, we may find support in the view of Faraday in his paper on the conservation of force (1858): "If in such strivings, we . . . see but imperfectly, still we should endeavour to see, for even an obscure and distorted vision is better than none. Let us, if we can, discover a new thing *in any shape*: the true appearance and character will be easily developed afterwards."

CXCII.—*The Diacyl Derivatives of Benzidine and* p-*Phenylenediamine.*

By Francis Joseph Anthony Brogan.

An alternation in melting point such as that shown by successive members of the normal fatty acid series has been found by Robertson (J., 1908, **93**, 1033; 1919, **115**, 1210) to occur to a more marked extent in the amides and various substituted amides; for the odd and the even members of each series, two distinct curves, more or less parallel, were obtained when the melting points were plotted against the number of carbon atoms in the acid chain. To explain this alternation of physical properties, the theory of alternating polarities has been put forward.

The melting points of two series of diacyl diamines, prepared by condensing the normal fatty acid chlorides with benzidine and *p*-phenylenediamine, respectively, have now been determined.

The diacyl diamines, with the exception of the diacetyl compounds, were prepared by the general method described by Robertson (*loc. cit.*). Dipropionyl- and dibutyryl-*p*-phenylenediamine could not be isolated, owing probably to their extreme solubility, but small amounts of the monoacyl compounds were obtained by adding light petroleum to aqueous-alcoholic solutions of the crude products. Recrystallisation of the crude product from aniline also gave the monoacyl compound.

The diacetyl compounds were prepared from acetic anhydride and the base in aqueous-alcoholic solution by Cain's method (J., 1909, **95**, 714). A considerable proportion of monoacyl compound also was formed.

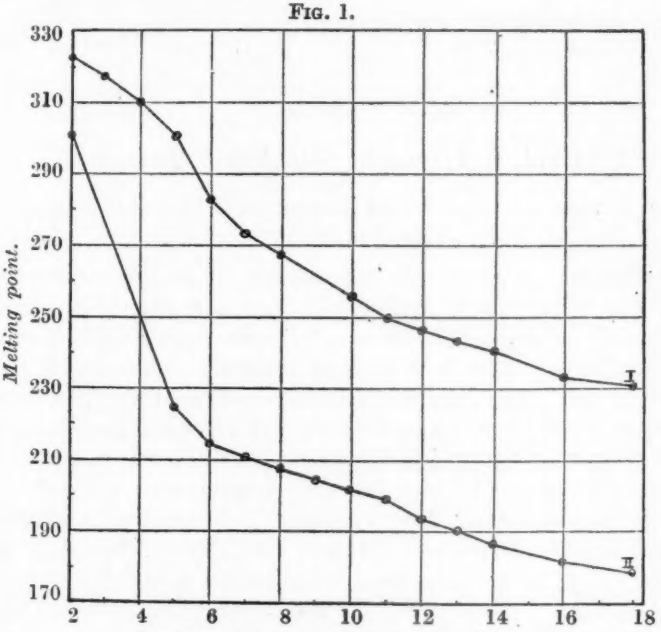
The crude products were recrystallised until the melting points were constant. The benzidine compounds, with the exception of the first three or four members of the series, are sparingly soluble in most of the common solvents. Alcohol was found to be the most suitable solvent for most of them, but the rate of solution was very slow, and prolonged boiling with a large volume of alcohol was necessary. Diacetylbenzidine crystallised well from aniline. The dipropionyl and dibutyryl compounds were very soluble in alcohol, and required to be precipitated by water. The four highest members were recrystallised from amyl acetate or acetic acid. The *p*-phenylenediamine derivatives, with the exceptions mentioned below, were recrystallised from alcohol, the solubility being much greater than that of corresponding compounds in the benzidine series. The diacetyl compound was recrystallised from nitrobenzene, and the two highest members from amyl acetate.

The new compounds prepared in this investigation, with their formulæ, melting points, and analytical results, are tabulated below.

Benzidine derivs.	M. p.	% N found.	*p*-Phenylenediamine derivs.	M. p.	% N found.
Dipropionyl, $C_{18}H_{20}O_2N_2$	317°	9·3	Divaleryl, $C_{16}H_{24}O_2N_2$	225°	10·3
Dibutyryl, $C_{20}H_{24}O_2N_2$	310	8·4	Dihexoyl, $C_{18}H_{28}O_2N_2$	215	9·1
Divaleryl, $C_{22}H_{28}O_2N_2$	301	7·7	Diheptoyl, $C_{20}H_{32}O_2N_2$	211	8·3
Dihexoyl, $C_{24}H_{32}O_2N_2$	283	7·3	Dioctoyl, $C_{22}H_{36}O_2N_2$	208	7·7
Diheptoyl, $C_{26}H_{36}O_2N_2$	274	6·7	Dinonoyl, $C_{24}H_{40}O_2N_2$	205	7·0
Dioctoyl, $C_{28}H_{40}O_2N_2$	268	6·4	Didecoyl, $C_{26}H_{44}O_2N_2$	202	6·6
Didecoyl, $C_{32}H_{48}O_2N_2$	256	5·5	Diundecoyl, $C_{28}H_{48}O_2N_2$	199	6·5
Diundecoyl, $C_{34}H_{52}O_2N_2$	250	5·4	Dilauryl, $C_{30}H_{52}O_2N_2$	194	5·9
Dilauryl, $C_{36}H_{56}O_2N_2$	247	4·9	Ditridecoyl, $C_{32}H_{56}O_2N_2$	190	5·6
Ditridecoyl, $C_{38}H_{60}O_2N_2$	243	4·9	Dimyristyl, $C_{34}H_{60}O_2N_2$	187	5·3
Dimyristyl, $C_{40}H_{64}O_2N_2$	241	4·6	Dipalmityl, $C_{38}H_{68}O_2N_2$	182	4·8
Dipalmityl, $C_{44}H_{72}O_2N_2$	233	4·3	Distearyl, $C_{42}H_{76}O_2N_2$	178	4·5
Distearyl, $C_{48}H_{80}O_2N_2$	231	4·1			

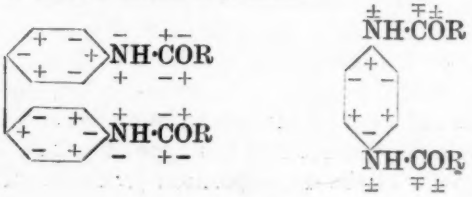
The results are shown graphically in the diagram, in which the melting points are plotted against the number of carbon atoms in the substituting acid. The general nature of the curves is typical, in so far as they fall fairly sharply at first and then more regularly with increase of molecular weight, but alternation is entirely absent. It is remarkable also that no minimum melting point is reached even at the eighteenth member, although a slight flattening is apparent about this point. Robertson's results indicate that the melting points become higher and the minimum occurs later as the molecule becomes heavier.

FIG. 1.



I. *Benzidine derivatives.* II. p-*Phenylenediamine derivatives.*

An examination of the polarity of the diacyl benzidines and *p*-phenylenediamines reveals the fact that a system of "crossed polarities" similar to that existing in the dibasic acids with an even number of carbon atoms is present.



This, together with the highly symmetrical nature of the molecule, would contribute to the structural stability of the acid, and thus tend to make the melting point high. The heaping up of like charges as in the odd dibasic acids, which may be supposed to make the crystalline arrangement less stable, and the melting points lower than those of the even acids, does not occur in the above compounds; this may explain the absence of alternation.

In conclusion, I wish to thank Professor Robertson for valuable advice and criticism in connexion with this research.

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CXCIII.—*Aromatic Sulphonyl Disulphides.*

By LESLIE GEORGE SCOTT BROOKER, REGINALD CHILD, and SAMUEL SMILES.

THE relative stability of incompletely oxidised sulphur chains attached to aromatic nuclei has not yet been systematically examined. Facts available from various sources show that so far as the dithio-system is concerned the fully oxidised chain of the disulphones is more resistant to fission than the partly oxidised group in the thiolsulphonates or in the unoxidised chain of disulphides. These relations, considered together with the labile character of the disulphide group in the tetrathio-compounds, $ArSO_2{\cdot}S_2{\cdot}SO_2Ar$, which spontaneously lose sulphur, yielding the corresponding monosulphides (Otto and Troger, *Ber.*, 1891, **24**, 1125), led to attempts to devise a method of introducing the thiolsulphonate group similar to that recently devised for inserting the thioaryl group (J., 1926, 1723). The experiments hitherto made with this object have chiefly dealt with the fission of substances containing the partly oxidised system $ArSO_2{\cdot}S{\cdot}S$— and have been devised to determine the mode of fission of this sulphur chain. If, as appeared probable for reasons such as those stated, the dithio-linking proved to be the less stable point of the sulphur complex, an intact thiolsulphonate group might survive the attack of suitable agents. The present investigation deals mainly with the diaryl sulphonyl disulphides. Although the desired method of synthesis of disulphoxides has not yet been attained, the results are now described, since this class of substance has not been previously encountered and their reactions illustrate the labile character of this type of sulphur chain and the varying character of the decomposition products. The substances

in question are readily obtained from the reaction of an aryl thiolsulphonate with a sulphur chloride,

$$ArSO_2{\cdot}SNa + SClAr = NaCl + ArSO_2{\cdot}S{\cdot}SAr,$$

and are well-defined materials which may be purified by the usual methods but decompose near their temperatures of fusion. Attempts to obtain these substances by partial oxidation of the more stable of the aromatic trisulphides or by reaction of a sulphinate with a disulphur chloride have not yet been successful. The sulphur chain in the aryl sulphonyl disulphides is easily broken by mercaptans, the chief product being the trisulphide corresponding to the mercaptan used (I). At the same time, fission of the dithio-system takes place in the reverse manner with the result that, when the aryl group of the mercaptan used is different from those present in the sulphonyl disulphide, unsymmetrical disulphides are formed (II). These modes of fission are summarised as follows :

(I.) $R^1SO_2{\cdot}\underset{H}{\overset{R^3S}{\underset{|}{\overset{|}{S}}}}{\cdot}\underset{SR^3}{\overset{H}{\underset{|}{\overset{|}{S}}}}{\cdot}SR^2$ $\qquad$ $R^1SO_2{\cdot}\underset{H}{\overset{|}{S}}{\cdot}\underset{SR^3}{\overset{SR^2}{\underset{|}{\overset{|}{S}}}}$ (II.)

(III.) $R^1SO_2{\cdot}\underset{Na}{\overset{C_{10}H_7O}{\underset{|}{\overset{|}{S}}}}{\cdot}\underset{C_{10}H_7O}{\overset{Na}{\underset{|}{\overset{|}{S}}}}{\cdot}SR^2$ $\qquad$ $R^1SO_2{\cdot}\underset{Na}{\overset{|}{S}}{\cdot}\underset{C_{10}H_7O}{\overset{SR^2}{\underset{|}{\overset{|}{S}}}}$ (IV.)

With sodium 2-naphthoxide or the sodium derivative of acetylacetone the unsymmetrical monosulphides are obtained (IV) together with 2-naphthol sulphide in the case of the first-named reagent (III), but since sodium mercaptide is liberated during these decompositions the symmetrical disulphide which is formed according to (II) is usually also encountered.

The behaviour of these reagents with the diarylsulphonyl monosulphides and trisulphides is similar. Thus ditoluenesulphonyl trisulphide was almost quantitatively decomposed by sodium 2-naphthoxide to 2-naphthol sulphide and toluenethiolsulphonate,

$$RSO_2{\cdot}S_3{\cdot}SO_2R \xrightarrow[C_{10}H_7{\cdot}ONa]{} 2RSO_2{\cdot}SNa + (C_{10}H_6{\cdot}OH)_2S,$$

and by sodium mercaptide to the trisulphide,

$$RSO_2{\cdot}S_3{\cdot}SO_2R \xrightarrow[R^1SNa]{} R^1{}_2S_3 + 2RSO_2{\cdot}SNa.$$

Ditoluenesulphonyl sulphide yielded 2-naphthol sulphide and the sulphinate

$$(RSO_2)_2S \xrightarrow[C_{10}H_7{\cdot}ONa]{O} 2RSO_2Na + (C_{10}H_6{\cdot}OH)_2S.$$

The trisulphides, sulphonyl disulphides and disulphonyl monosulphides form an interesting series in which the trithio-system

occurs in successive stages of oxidation, but at present it is inadvisable to discuss the relative stability of these, since experience has shown that in each class this may vary with the nature of the substituents in the aromatic nuclei, and precise information concerning this factor is lacking.

Experimental.

The sulphonyl disulphides were prepared by shaking the finely powdered potassium thiolsulphonate with dry ether containing the theoretical amount of aryl sulphur chloride. Interaction was usually rapid and when it was complete the solid was collected and washed with water; the residue, containing the desired material, was then purified from a suitable solvent. A further quantity of the sulphonyl disulphide could in most cases be obtained from the ethereal solution. In this way, the following derivatives were obtained; they are numbered for the purpose of reference on a subsequent page.

I. 4-*Toluenesulphonyl* 2-*nitrophenyl disulphide*,

$$C_7H_7\cdot SO_2\cdot S\cdot S\cdot C_6H_4\cdot NO_2,$$

formed yellow plates, m. p. 141°, from acetic acid (Found: S, 28·3; *M*, 336. $C_{13}H_{11}O_4NS_3$ requires S, 28·2%; *M*, 341).

II. 4-*Acetamidobenzenesulphonyl* 2-*nitrophenyl disulphide*,

$$NHAc\cdot C_6H_4\cdot SO_2\cdot S\cdot S\cdot C_6H_4\cdot NO_2,$$

separated from acetone in yellow needles, m. p. 171° (decomp.) (Found: C, 43·8; H, 3·1; S, 24·9. $C_{14}H_{12}O_5N_2S_3$ requires C, 43·7; H, 3·1; S, 25·0%).

III. 4-*Toluenesulphonyl* 4-*chloro*-2-*nitrophenyl disulphide*,

$$C_7H_7\cdot SO_2\cdot S\cdot S\cdot C_6H_3Cl\cdot NO_2,$$

was obtained from hot alcohol in yellow needles, m. p. 114° (Found: C, 41·6; H, 2·9; Cl, 9·3; S, 25·5. $C_{13}H_{10}O_4NClS_3$ requires C, 41·5; H, 2·9; Cl, 9·4; S, 25·6%).

IV. 4-*Toluenesulphonyl* 2 : 5-*dichlorophenyl disulphide*,

$$C_7H_7\cdot SO_2\cdot S\cdot S\cdot C_6H_3Cl_2,$$

separated from benzene–light petroleum in prisms, m. p. 95—96° (Found: C, 42·7; H, 2·7; Cl, 19·3; S, 26·1. $C_{13}H_{10}O_2Cl_2S_3$ requires C, 42·7; H, 2·8; Cl, 19·4; S, 26·3%).

V. 4-*Methoxytoluene*-3-*sulphonyl* 2-*nitrophenyl disulphide*,

$$MeO\cdot C_6H_3Me\cdot SO_2\cdot S\cdot S\cdot C_6H_4\cdot NO_2,$$

has m. p. 115—116° (Found: C, 45·2; H, 3·7; S, 25·4; *M*, 362. $C_{14}H_{13}O_5NS_3$ requires C, 45·2; H, 3·5; S, 25·9%; *M*, 371).

VI. 4-*Chlorobenzenesulphonyl* 2-*nitrophenyl disulphide*,

$$C_6H_4Cl\cdot SO_2\cdot S\cdot S\cdot C_6H_4\cdot NO_2,$$

formed yellow plates from acetic acid; m. p. 147° after softening at about 130° (Found: C, 39·9; H, 2·4; Cl, 9·9; *M*, 352. $C_{12}H_8O_4NClS_3$ requires C, 39·8; H, 2·2; Cl, 9·8%; *M*, 361·5).

The interaction of these substances with the reagents mentioned was effected in boiling alcohol which contained two molecular proportions of the mercaptan or sodium 2-naphthoxide and one of the sulphonyl disulphide. When the reaction was complete, the alcohol was evaporated and the residue was extracted with water. The further separation of the products varied according to the nature of the reactants. Identification of the products was effected by comparison with authentic specimens from other sources; when the substances had not been previously described, they were prepared for comparison by other methods. In the following summary the numerals refer to the sulphonyl disulphides described above.

I, with the sodium derivative of acetylacetone, yielded 2-nitrophenyl disulphide and 2-nitrophenyl acetylacetonyl sulphide, m. p. 136—137° (J., 1926, 1727). From the interaction with 2 : 5-dibromophenyl mercaptan the corresponding trisulphide and 2 : 5-dibromophenyl 2-nitrophenyl disulphide were isolated. 2 : 5-*Dibromophenyl trisulphide*, m. p. 167—168°, formed needles from benzene (Found: Br, 56·5. $C_{12}H_6Br_4S_3$ requires Br, 56·5%) and was also prepared from the mercaptan and sulphur dichloride in carbon tetrachloride. 2 : 5-*Dibromophenyl 2-nitrophenyl disulphide*, $C_6H_3Br_2{\cdot}S{\cdot}S{\cdot}C_6H_4{\cdot}NO_2$, was also obtained from the dibromophenyl mercaptan and 2-nitrophenyl sulphur chloride. It formed yellow prisms, m. p. 138°, from acetic acid (Found: Br, 38·1. $C_{12}H_7O_2NBr_2S_2$ requires Br, 38·0%).

III, with sodium 2-naphthoxide, yielded 2-naphthol sulphide, toluenesulphinic acid, 4-chloro-2-nitrophenyl disulphide, and 4-chloro-2-nitrophenyl 2-naphthol sulphide (I) (Found: Cl, 10·3. Calc.: Cl, 10·7%).

IV, with 2-nitrophenyl mercaptan, gave 2-nitrophenyl trisulphide (Lecher, *Ber.*, 1922, **55**, 2423) and 2 : 5-*dichlorophenyl 2-nitrophenyl disulphide*, $C_6H_3Cl_2{\cdot}S{\cdot}S{\cdot}C_6H_4{\cdot}NO_2$, which was also prepared from 2-nitrophenyl sulphur chloride and 2 : 5-dichlorophenyl mercaptan, and separated from hot acetic acid in yellow needles, m. p. 138° (Found: C, 43·3; H, 2·1. $C_{12}H_7O_2NCl_2S_2$ requires C, 43·2; H, 2·2%).

V, with 2 : 5-dichlorophenyl mercaptan, yielded 2 : 5-dichlorophenyl 2-nitrophenyl disulphide, 4-methoxytoluene-3-sulphinic acid, and 2 : 5-*dichlorophenyl trisulphide*, $(C_6H_3Cl_2)_2S_3$, which formed needles, m. p. 140°, from acetic acid (Found: Cl, 36·2. $C_{12}H_6Cl_4S_3$ requires Cl, 36·5%). This substance was also obtained from the mercaptan and sulphur chloride; by hydrogen peroxide in acetic acid at 100°, it was converted into 2 : 5-dichlorophenyl disulphoxide.

VI, with the sodium derivative of acetylacetone, yielded 2-nitro-

phenyl disulphide, 4-chlorobenzenesulphinic acid, and 2-nitrophenyl acetylacetonyl sulphide.

4-Toluenesulphonyl trisulphide or 4-toluenesulphonyl sulphide was decomposed in boiling alcohol by sodium 2-naphthoxide (2 mols.). The products were as stated in the theoretical part. Sodium 4-toluenethiolsulphonate, formed from the first-named sulphide, was identified by conversion into 4-toluenesulphonyl 4-chloro-2-nitrophenyl disulphide.

In conclusion, we desire to thank the Department of Scientific and Industrial Research for a grant which has enabled one of us (L. G. S. B.) to take part in these experiments.

KING'S COLLEGE, LONDON. [*Received, April 28th*, 1927.]

CXCIV.—*The Dicarbazyls. Part III. The Oxidation of Carbazole and N-Alkylcarbazoles in Acid Solution.*

By PETER MAITLAND and STANLEY HORWOOD TUCKER.

PERKIN and TUCKER (J., 1921, **119**, 216) have described three products of the oxidation of carbazole by potassium permanganate in acetone solution. Two of these were crystalline, A, m. p. 220°, and B, m. p. 265°, and the third amorphous, m. p. about 175°. A and B were proved to be dicarbazyls, the constitutions, however, being unknown; neither is 3 : 3′-dicarbazyl, since synthesised by Tucker (J., 1926, 3033). McLintock and Tucker (this vol., p. 1214) have shown that A is 9 : 9′-dicarbazyl.

In the present research, by oxidising 9-methylcarbazole, we made sure that, in any dicarbazyl produced, the two carbazole nuclei would be united by a bond between two carbon atoms. 9-Methylcarbazole was unaffected in acetone solution by potassium permanganate. Oxidation by Wieland's method (*Ber.*, 1913, **46**, 3296), however, gave 9 : 9′-dimethyl-3 : 3′-dicarbazyl, the constitution of which was proved by its preparation from 3 : 3′-dicarbazyl by direct methylation. These results were confirmed by analogous experiments on 9-ethylcarbazole, 9 : 9′-diethyl-3 : 3′-dicarbazyl being obtained. In both these oxidations there was no evidence of the formation of any isomeric 1 : 1′- or 1 : 3′-dicarbazyl.

The fact that no 3 : 3′-dicarbazyl was formed in Perkin and Tucker's oxidation of carbazole led us to attempt the oxidation by other methods. Carbazole, when oxidised in boiling acetic acid with sodium dichromate, gave a product which contained chromium. When, however, the :NH group was protected by sulphuric acid,

no chromium-containing products were obtained. Although no sulphate of carbazole has been isolated, it appears to exist under the experimental conditions employed, since oxidation by Wieland's method gave 3 : 3′-dicarbazyl, uncontaminated with any 9 : 9′-dicarbazyl.

The mechanism of the acid oxidation of carbazole was thought to be closely allied to that of the corresponding oxidation of diphenylamine to diphenylbenzidine (Wieland, *Ber.*, 1913, **46**, 3296. *o*-Nitrodiphenylamine gives, correspondingly, *NN′*-di-*o*-nitrophenylbenzidine; Tucker, *loc. cit.*, 3034). Two theories of the mechanism of this oxidation have been put forward : (1) That the benzene nuclei unite directly, without the formation of an intermediate product (Wieland); (2) that the primary attack occurs at the :NH group with the formation of an intermediate compound which subsequently undergoes transformation (Marqueyrol and Muraour, *Bull. Soc. chim.*, 1914, **15**, 191).

(1) In support of this assumption, Wieland has shown that tetraphenylbenzidine is formed by the oxidation of triphenylamine. This evidence is not conclusive, because the oxidation is effected in acetic acid solution, whereas in the case of diphenylamine the presence of sulphuric acid is necessary, and also because of the introduction of the acidic phenyl group. We have, however, been able to oxidise *N*-methyldiphenylamine in sulphuric acid solution to *NN′*-dimethyldiphenylbenzidine, $NMePh{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NMePh$. The intermediate formation of an N—N-compound is here excluded; oxidation brings about direct C—C-linking. This is in complete agreement with Wieland's view.

(2) The investigations of Marqueyrol and Muraour have led them to the conclusion that the sulphuric acid is only necessary, in that it causes the transformation of an intermediate product. (The constitution of this intermediate product is unknown, but it has been shown that it cannot be tetraphenylhydrazine.) They base their conclusions on oxidation experiments in which they protected the NH group by varying quantities of concentrated sulphuric acid, and found that the amount of recovered diphenylamine increased with increase in the amount of concentrated sulphuric acid used. We have repeated their experiments, and have found that the amount of unchanged diphenylamine is negligible. There seems, therefore, to be no valid experimental work against the view of Wieland. Furthermore, in the analogous acid oxidation of carbazole to give 3 : 3′-dicarbazyl, the evidence is against the intermediate formation of 9 : 9′-dicarbazyl, since the transformation of 9 : 9′-dicarbazyl into 3 : 3′-dicarbazyl cannot be brought about (McLintock and Tucker, *loc. cit.*). Again, the oxidation of 9-methyl-

and of 9-ethyl-carbazole to the corresponding 3 : 3′-dicarbazyl derivatives cannot take place through the intermediate formation of a 9 : 9′-dicarbazyl.

In all the acid oxidations of carbazole and its derivatives, and also in the acid oxidation of *N*-methyldiphenylamine, brightly coloured substances are produced. We suggest that these substances possess quinonoid structures, and are similarly constituted to the analogously formed oxidation products of diphenylamine (Kehrmann and Micewicz, *Ber.*, 1912, **45**, 2641).

Experimental.

Oxidation of 9-Methylcarbazole by Wieland's Method (modified).—Methylcarbazole (5 g.) was dissolved in a mixture of glacial acetic acid (200 c.c.) and sulphuric acid (5 c.c.), and sodium dichromate (6·5 g.; 1½ times the theoretical quantity) dissolved in the smallest quantity of water was added during 1 minute, the whole being cooled in ice. The solution turned bluish-green immediately, and a precipitate formed. After 10 minutes, the solution was poured into an equal bulk of a concentrated solution of sodium bisulphite, and heated on the water-bath until the blue colour disappeared. The green precipitate obtained was removed and extracted with benzene; the residue (0·5 g.) contained chromium. The concentrated, hot benzene solution was poured into twice its volume of hot alcohol to remove unchanged 9-methylcarbazole. The light brown, crystalline mass, deposited over-night, was dissolved in hot acetic anhydride, and glacial acetic acid added, followed by zinc dust. After boiling for 10 minutes, the dark brown solution lightened in colour; it was filtered, and the filtrate poured cautiously into ammonia solution (ammonia, *d* 0·88, diluted with its own bulk of water). The slightly coloured mass deposited was crystallised three times from benzene (charcoal). Slightly pink needles of *9 : 9′-dimethyl-3 : 3′-dicarbazyl*, m. p. 200—202°, were obtained (Found: C, 86·4; H, 5·6; N, 7·8; *M*, cryoscopic in benzene, 380, 375. $C_{26}H_{20}N_2$ requires C, 86·7; H, 5·6; N, 7·8%; *M*, 360).

Oxidation of 9-Ethylcarbazole.—9-Ethylcarbazole (20 g.), glacial acetic acid (1 litre), sulphuric acid (25 c.c.), and sodium dichromate (12·8 g.) were used as in the preceding oxidation. The residue (2 g.) after the extraction with benzene contained chromium. The benzene solution was concentrated and poured into hot alcohol (400 c.c.). The brown, crystalline mass deposited over-night (16 g.) melted at 174—176°. It was purified as described above and cream-coloured prisms of *9 : 9′-diethyl-3 : 3′-dicarbazyl*, m. p. 188—190°, were obtained (Found: C, 86·5; H, 6·4; N, 7·2; *M*, by Rast's method, 342, 391. $C_{28}H_{24}N_2$ requires C, 86·6; H, 6·2 N, 7·2%; *M*, 388).

Excellent yields of the crude alkylated dicarbazyls were obtained, but great difficulty was experienced in isolating the pure dicarbazyls. Fractional crystallisation from benzene, toluene, xylene, acetic anhydride, or pyridine, in which the dicarbazyls are very soluble, and also from acetic acid, alcohol, or acetone, in which they are sparingly soluble, was tried in the attempt to isolate an isomeride. Sublimation in a vacuum or treatment with potassium permanganate in acetone solution had little effect. There was no evidence of the presence of any 1 : 1′- or other isomeride.

Oxidation of Carbazole.—The procedure used in the oxidation of 9-methylcarbazole (above) was followed, pure carbazole (5 g.), glacial acetic acid (1250 c.c.), sulphuric acid (30 c.c.), and sodium dichromate (3·2 g.) being employed. After the heating following the addition of the bisulphite (1 litre), the solution was further diluted and left over-night. The light brown, flocculent precipitate was washed, dried, and extracted with anisole (500 c.c.); the green residue (1 g.) did not contain chromium. The dark brown filtrate was concentrated and boiled with charcoal; 3 : 3′-dicarbazyl (1·7 g.), m. p. over 300°, was then obtained in colourless microcrystals. Its acetyl derivative was identical with that of synthetic 3 : 3′-dicarbazyl (Tucker, *loc. cit.*).

Methylation of 3 : 3′-*Dicarbazyl* (Stevens and Tucker's method, J., 1923, **123**, 2140).—3 : 3′-Dicarbazyl (0·8 g.) was suspended in acetone (40 c.c.), methyl sulphate (2 c.c.) added, and then powdered potassium hydroxide (2 g.). Water was added drop by drop until the potash formed a layer. After boiling for 10 minutes, the solution was poured into water, and the precipitate obtained was washed, dried, and crystallised from benzene three times, giving white needles, m. p. 198—200°. This substance was identical with 9 : 9′-dimethyl-3 : 3′-dicarbazyl prepared by oxidation of 9-methylcarbazole.

Ethylation of 3 : 3′-*Dicarbazyl.*—3 : 3′-Dicarbazyl (0·4 g.) was suspended in acetone (30 c.c.), and ethyl sulphate (5 c.c.) added; powdered potassium hydroxide (10 g.) was then added in small quantities to the boiling solution. On pouring the mixture into water, an oil was obtained (due to the large amount of potash acting on the acetone). After steam distillation, the solid residue was crystallised four times from benzene, and shown to be 9 : 9′-diethyl-3 : 3′-dicarbazyl.

Oxidation of N-*Methyldiphenylamine.*—*N*-Methyldiphenylamine (prepared as described by Gibson and Vining, J., 1923, **123**, 835, and further purified by steam distillation) (5 g.) was dissolved in a cold mixture of concentrated sulphuric acid (20 c.c.) and water (50 c.c.). To the pale yellow solution, sodium dichromate (1·35 g.), dissolved

in water (10 c.c.), was added drop by drop with shaking. A reddish-violet coloration was produced, but was rapidly discharged, and a white precipitate separated. Decoloration was more rapid as the solution became warm. When the last few drops of the dichromate solution had been added (*i.e.*, slight excess over the amount theoretically required), the mauve colour persisted. The colour was removed by treating the mixture with a few drops of sulphurous acid. The separated, salmon-coloured substance (5 g.) was extracted with benzene. Part remained insoluble. The concentrated benzene extract deposited faintly green crystals, which, after several recrystallisations from benzene and finally from acetone, gave white, nacreous laminæ, softening at 167° and melting at 170°, of NN′-*dimethyldiphenylbenzidine* (Found: C, 85·9; H, 6·8; N, 7·9; *M*, by Rast's method, 386. $C_{26}H_{24}N_2$ requires C, 85·7; H, 6·6; N, 7·7%; *M*, 364). On account of the necessary repeated crystallisations the yield of pure product (1·5 g.) was low. No isomeride could, however, be isolated. Crystallisation from ethyl acetate or acetone, without previous use of benzene, failed to purify the product. All solutions possess a faint violet fluorescence.

It crystallises from the usual organic solvents, but is insoluble in alcohol or light petroleum.

N-Methyldiphenylamine, by oxidation with potassium permanganate in acetone, gave *NN′*-dimethyldiphenylbenzidine in small yield.

Methylation of Diphenylbenzidine.—*NN′*-Diphenylbenzidine (1 g.) was dissolved in methyl sulphate (10 c.c.) by warming on the water-bath for 15 minutes. A solution of sodium carbonate in water (35 g. in 200 c.c.) was added during 1 hour, the temperature being kept between 50° and 60°. An oil separated and solidified on cooling. After being washed and dried, the solid was extracted with benzene. Crystals eventually obtained were identical with those of *NN′*-dimethyldiphenylbenzidine prepared by oxidation of *N*-methyldiphenylamine.

UNIVERSITY OF GLASGOW. [*Received, April 22nd*, 1927.]

CXCV.—*Acid Soaps: A Crystalline Potassium Hydrogen Dioleate.*

By JAMES WILLIAM MCBAIN and ALEXANDER STEWART.

No acid soaps of definite composition have been shown to exist, although the analogous acid sodium acetates ($NaC_2H_3O_2,C_2H_4O_2$, and $NaC_2H_3O_2,2C_2H_4O_2$) have long been known. The present paper describes the preparation of the first definite crystalline compounds of this type observed with the soaps.

Potassium hydrogen dioleate was first prepared from oleic acid "Kahlbaum" and a special Kahlbaum preparation of potassium oleate. These were dissolved in distilled alcohol, and upon cooling with ice a crystalline deposit was obtained. Two or three recrystallisations completely removed any brown colour. The crystals were dried, after being washed with ice-cold alcohol, in a vacuum desiccator over fused calcium chloride for 8—10 days; they then attained constant weight and the analysis was not altered by further drying at 40° in a vacuum.

The acid soap was analysed as follows. To a weighed quantity of solution contained in a stoppered flask a measured excess of standard hydrochloric acid was added slowly from a pipette with vigorous stirring. The precipitated fatty acid was allowed to stand over-night, for the resulting emulsion to clear, and then filtered off through wetted filter-paper and washed free from hydrochloric acid with boiled-out distilled water. The filtrate was titrated with standard sodium hydroxide and phenolphthalein; the difference between this and the amount of hydrochloric acid originally taken determines the total concentration of soap and hydroxide. The fatty acid on the filter paper was dissolved in boiled-out alcohol and titrated with sodium hydroxide, which had been standardised both against the oleic acid used and against hydrochloric acid (Hulett and Bonner, *J. Amer. Chem. Soc.*, 1909, **31**, 345), more boiled-out alcohol being added, if necessary, in order to maintain an alcohol concentration of 70—80%. Determinations of saponification value gave results in good agreement with this method of analysis.

The procedure ultimately adopted was to obtain crystals of acid soap from alcoholic solutions containing various proportions of potassium oleate and oleic acid. The analyses in the table show that the crystals contained one equiv. of oleic acid to one equiv. of potassium oleate, and that the composition over a wide range was independent of the proportions in the alcohol. In each case, 3—4 g. of acid soap were taken for analysis and about 6 g. for saponification values. The amounts of oleate and potassium found by analysis agreed with the total weight of sample taken within 0·2%.

Analysis of crystals obtained from alcoholic solutions of potassium oleate and oleic acid in various proportions.

Propn. in alc.	Ratio in crystal (Oleate/K).	Mol. wt. from saponification value.
KOl : 2HOl.	2·011	—
KOl : HOl.	2·007, (1·952), 1·980, 1·990, 1·986, 2·006, 2·005	600, 600·4
2KOl : HOl.	—	602·6, 601·9
3KOl : HOl.	—	903·1, 905·7
	Theory for KOl : HOl =	602·6
	" " 2KOl : HOl =	923·1

The following method of preparation was found convenient: 130 G. of oleic acid and 145 g. of potassium oleate are dissolved in alcohol by warming, diluted to a litre, and allowed to crystallise at 0°. The white crystals are recrystallised 3 or 4 times—the last time only, from dry alcohol. Drying is completed in a vacuum over frequently-changed fused calcium chloride. This process not only removes the colour, if impure oleic acid is used, but results in definite purification.

The acid soap may be recrystallised from pure oleic acid instead of alcohol; the ratio of oleate to potassium in such a recrystallised product, dried in a screw press with renewed layers of filter paper, was found by analysis to be 2·026 and 2·004.

Potassium hydrogen dioleate forms well-defined crystalline plates; the photograph (Fig. 1) shows a typical group of crystals with dark-ground illumination. This compound possesses a transition point at 43°, at which temperature the solid partly liquefies, and it is only upon heating the system to above 107° that it again becomes homogeneous, giving a clear liquid.

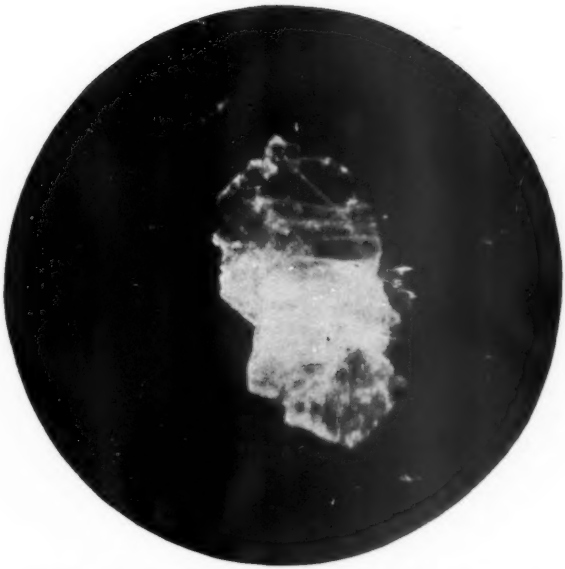
In order to determine whether potassium oleate or a second acid soap was the decomposition product, a quantity of the crystals was placed in a screw press between a number of filter-papers, and kept in an oven at 55—60°, the filter-papers being changed until no more oily liquid was removed from the press cake. Analysis of the product showed that the ratio of oleate radical to potassium was 1·001. Thus the decomposition product at 55° is neutral potassium oleate, the other phase being a liquid solution of potassium oleate in oleic acid.

Further communications will contain the results of phase-rule investigations in the two-component systems soap–fatty acid and the three-component systems soap–fatty acid–water.

Summary.

A definite crystalline compound, anhydrous potassium hydrogen dioleate, has been obtained, showing a transition point at 43° at which it breaks up into potassium oleate and a liquid solution of oleate and oleic acid. It crystallises unaltered from oleic acid or from various compositions of alcoholic solution. It offers a means of purification of oleic acid.

UNIVERSITY OF BRISTOL. [*Received, December 20th*, 1926.]



Crystal of potassium hydrogen dioleate. Oblique illumination. Magnification × 100.

[*To face p.* 1394.]

CXCVI.—*The Action of Nitrous Acid on Substituted* p-*Phenylenediamines. Part I. Benzyl*-n-*butyl*-p-*phenylenediamine.*

By Joseph Reilly and Peter J. Drumm.

Butyl-*p*-phenylenediamine behaves normally on diazotisation (Reilly and Hickinbottom, J., 1917, **111**, 1034). According to Hantzsch (*Ber.*, 1902, **35**, 896), methyl-*p*-phenylenediamine cannot be readily diazotised in hydrochloric acid solution, nitrogen being evolved even below 0°; the present authors have found, however, that a much more stable diazo-solution is obtained if sulphuric acid is used. Substituents in aromatic diamines therefore have a marked influence on the stability of the diazo-solutions produced from them, and in view of this the authors have commenced an investigation on the nature of the reaction between nitrous acid and various mono- and di-substituted diamines and on the stability of the resulting solutions.

Benzyl-n-*butyl*-p-*phenylenediamine*, $NH_2 \cdot C_6H_4 \cdot N(C_4H_9) \cdot CH_2Ph$, the first diamine to be investigated, was obtained from *benzyl*-n-*butylaniline* through the p-*nitroso*-compound and also by reduction of the azo-compound formed by coupling this tertiary amine with diazosulphanilic acid. It diazotises readily to give a comparatively stable diazo-solution.

Experimental.

Benzyl-n-*butylaniline*.—Benzylaniline (1 mol.) and *n*-butyl iodide (1 mol.) were heated together at 100° for 6 hours, the excess of *n*-butyl iodide was removed under diminished pressure, and the residue made alkaline with aqueous sodium hydroxide. The resulting oil was dissolved in ether and dried with potassium carbonate. The fraction, b. p. 190—200°/17 mm., on refractionation gave *benzyl*-n-*butylaniline* as a pale yellow oil, b. p. 193—195°/17 mm., $d^{16\cdot5}$ 1·005 (yield, 20%). It possesses feebly basic properties and is very sparingly soluble in dilute acids. The *picrate* forms bright yellow prisms, m. p. 129° (Found: $C_6H_3O_7N_3$, 49·3. $C_{17}H_{21}N,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 48·9%), and is decomposed by boiling water. The *chloroplatinate* is only slightly soluble in alcohol, from which it separates in biscuit-coloured prisms, m. p. 185—186° (decomp.) [Found: Pt, 21·8. $(C_{17}H_{22}N)_2PtCl_6$ requires Pt, 21·9%].

p-*Nitrosobenzyl*-n-*butylaniline*.—A well-cooled solution of benzyl-*n*-butylaniline in glacial acetic acid was slowly treated with a solution of the theoretical quantity of sodium nitrite in the minimum

of water. The mixture was stirred for 3 hours and then diluted with ice-water, and the precipitated green oil was dissolved in benzene. From the dried, cooled benzene solution, hydrogen chloride precipitated p-*nitrosobenzyl*-n-*butylaniline hydrochloride*; this, after being washed with benzene, dissolved in absolute alcohol, and reprecipitated by ether, was obtained in greenish-yellow, glistening plates, m. p. 138° with previous darkening (Found: Cl, 11·8. $C_{17}H_{20}ON_2$,HCl requires Cl, 11·6%). It is readily hydrolysed by water.

The *base* was obtained by decomposing the hydrochloride with aqueous sodium carbonate; it crystallised from ether in green, glistening plates, m. p. 48—49°, which appeared steel-blue by reflected light (Found: N, 10·0. $C_{17}H_{20}ON_2$ requires N, 10·4%). When it was heated with concentrated hydrochloric acid, a pronounced odour of benzaldehyde was observed. On reduction with zinc dust and dilute sulphuric acid, it gave *benzyl*-n-*butyl*-p-*phenylenediamine*, which is described below.

4-p-*Sulphobenzeneazobenzyl*-n-*butylaniline*.—Solid diazosulphanilic acid was gradually added to a glacial acetic acid solution of benzyl-*n*-butylaniline. The mixture was shaken for 3 hours and diluted with water; the *azo*-compound then separated in well-defined, violet crystals (Found: S, 7·7. $C_{23}H_{25}O_3N_3S$ requires S, 7·6%). It forms a very soluble, orange *sodium* salt.

Benzyl-n-*butyl*-p-*phenylenediamine*.—Reduction of the preceding azo-compound (20 g.) by ammonium sulphide solution proceeded in the cold and was complete at the end of 24 hours. The precipitated oil was dissolved in ether, the solution washed with an aqueous suspension of lead carbonate to remove traces of ammonium sulphide, and the ether distilled off; *benzyl*-n-*butyl*-p-*phenylenediamine* was then obtained at 220—224°/12 mm. as a pale yellow oil (yield, 75%) (Found: N, 10·6. $C_{17}H_{22}N_2$ requires N, 11·0%), which slowly became red in the air.

The *sulphate* was obtained as a white solid from sulphuric acid and the amine in ethereal solution [Found: S, 5·6. $(C_{17}H_{22}N_2)_2,H_2SO_4$ requires S, 5·3%]. It is very soluble in alcohol and water. The *hydrochloride* was similarly prepared and obtained as a very hygroscopic, viscous precipitate. The *benzoyl* compound, prepared by the Schotten–Baumann reaction, was obtained in colourless needles, m. p. 131° (Found: N, 8·1. $C_{24}H_{26}ON_2$ requires N, 7·8%).

p-*Benzyl*-n-*butylaminobenzeneazo*-β-*naphthol*.—The green solution obtained by diazotising benzyl-*n*-butyl-*p*-phenylenediamine (prepared in either of the two ways mentioned above) in hydrochloric acid solution was freed from nitrous acid by means of carbamide and added to an alkaline solution of β-naphthol. The brown precipitate

thus produced crystallised from alcohol in stout, dark red prisms with a greenish lustre; m. p. 133—134° (Found by the micro-method: N. 10·3. $C_{27}H_{27}ON_3$ requires N, 10·3%). With concentrated sulphuric acid, it developed a magenta colour, which changed to yellowish-orange on dilution.

The authors wish to thank the Research Fund Committee of the Chemical Society for a grant which has partly defrayed the cost of this work.

UNIVERSITY COLLEGE, CORK. [*Received, April 7th*, 1927.]

NOTES

The Estimation of Potassium in Presence of Iodide. By FRANK SWAIN HAWKINS and JAMES RIDDICK PARTINGTON.

THE estimation of potassium in presence of iodides is not easy. The cobaltinitrite method gives too high results. The chloroplatinate method cannot be used unless the iodide is first removed. When this is effected by cupric sulphate and sulphur dioxide, followed by precipitation of excess copper with sodium hydroxide, the results are low. Removal of iodide by silver nitrate, followed by hydrochloric acid to remove excess of silver, gives high results (102·3—105·4%). Reduction of the chloroplatinate obtained by any method to platinum by means of magnesium is unsatisfactory, since no specimen of magnesium used was completely soluble in hydrochloric acid. There is also the difficulty of the uncertain composition of the chloroplatinate precipitate (see Treadwell, "Quantitative Analyse," 1919, 39 ff.; the method given in the English translation is unsatisfactory). A modification of the perchlorate method was finally adopted. When an alkali iodide is evaporated to dryness with perchloric acid a sufficient number of times, the whole of the iodine can be expelled, but there is loss probably due to the fumes carrying over solid particles mechanically. Evaporation to the fuming point is insufficient. The following method gave good results. A saturated solution of potassium perchlorate in 96% alcohol is cooled to 0° and filtered. A saturated solution of sodium perchlorate is similarly prepared. The alkali iodides are dissolved in the alcohol saturated with potassium perchlorate, sufficient of the sodium perchlorate solution is added to precipitate all the potassium, and the solution is boiled, cooled to 0°, and filtered through a Gooch crucible. The precipitate is

washed with the alcoholic potassium perchlorate at 0°, dried at 360°, and weighed. This gave results of the order of 99·95% with pure potassium iodide, the only error being due to a tendency of the precipitate to adhere to glass. By this method the sources of error described by Smith and Ross (*J. Amer. Chem. Soc.*, 1925, **47**, 774) are avoided. The method can be used for any potassium salts soluble in 96% alcohol.—EAST LONDON COLLEGE, UNIVERSITY OF LONDON. [*Received, May* 11th, 1927.]

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o-Nitrobenzylphenyldimethylammonium Chloride. By HLA BAW.

THE *m*- and *p*-nitro-isomerides of this compound have already been described (Wedekind, *Annalen*, 1899, **307**, 287; Peacock, *J. Soc. Dyers and Col.*, 1926, 53). When *o*-nitrobenzyl chloride and dimethylaniline in equivalent quantities were mixed and kept for some months, they slowly combined to form the *quaternary compound*, which separated in large, rhomboid crystals. These were washed with ether and recrystallised from alcohol–ether. The substance had a faintly yellow colour and turned green superficially on keeping; m. p. 99·5° (Found: Cl, 11·8, 11·6. $C_{15}H_{17}O_2N_2Cl$ requires Cl, 12·1%).—UNIVERSITY COLLEGE, RANGOON, BURMA. [*Received, April 25th*, 1927.]

A Spectrographic Method for the Determination of Dissociation Constants. By R. A. MORTON and A. H. TIPPING.

IT has been shown that the visible colour of solutions of violuric acid is due entirely to the violurate ion (J., 1925, **127**, 2514). Control determinations of p_H values with the quinhydrone electrode have enabled us to arrive at the value $e = 60$ for the extinction coefficient of a gram-ion of the acid radical. Hence it follows that, with a known initial concentration of violuric acid, the equation

$$K = [H^+][Vi^-]/[HVi_{undiss.}] = [Vi^-]^2/([HVi_{total}] - [Vi^-]) \quad . \quad . \quad (1)$$

allows of the evaluation of the dissociation constant from a spectroscopic determination of the concentration of the violurate ion.

For example, a solution of 0·00306*N*-violuric acid in a 30 cm. cell has *e* max. 0·42 at the position of maximum absorption. From the relation $\log I_0/I = ecd$, $0{\cdot}42 = 60 \times x \times 30$; *i.e.*, x, the concentration of violurate ion, = 0·000233. Hence $K = (0{\cdot}000233)^2/(0{\cdot}00306 - 0{\cdot}000233)$ or $1{\cdot}92 \times 10^{-5}$.

A simple extension of this work enables us to determine the dissociation constants of weak acids which obey the dilution law: If for a mixture of violuric acid of concentration [HVi] with another acid of concentration [HA] the value of $\log I_0/I$ at the position

of maximum absorption is found, it is clear from the relation $\log I_0/I = ecd$ that the concentration of the violurate ion can be obtained. [HVi] and [Vi$^-$] are thus known, so that the concentration [HVi$_{\text{undiss.}}$] of the undissociated acid follows. From equation (1) [H$^+$] can be determined, since K is known. The mixture is electrically neutral, so that [H$^+$] = [Vi$^-$] + [A$^-$] + [OH$^-$]. In acid solutions [OH$^-$] is negligible, so that [H$^+$] = [Vi$^-$] + [A$^-$]. In this equation [A$^-$] is the only unknown quantity and can therefore be evaluated. The concentration [HA] originally used is known, so that [HA$_{\text{undiss.}}$] = [HA] − [A$^-$]. Hence K_{HA} = [H$^+$][A$^-$]/[HA$_{\text{undiss.}}$].

The following results were obtained :

Acid.	K.	Standard values.
Acetic	1·5—1·8 × 10^{-5} at 18°	1·82 × 10^{-5} at 18°
„	1·5—1·9 × 10^{-5} at 19°	„
„	1·7—2·0 × 10^{-5} at 20°	„
Chloroacetic	1·4—1·7 × 10^{-3} at 18·5°	1·55 × 10^{-3} at 25°
Glycollic	1·3—1·6 × 10^{-4} at 19°	1·5 × 10^{-4} at 25°
Salicylic	1·0—1·2 × 10^{-3} at 19°	1·04 × 10^{-3} at 20°

The method can also be extended to the determination of the distribution of a base between violuric acid and another weak acid. This has been verified for mixtures of acetic and violuric acids.—The University, Liverpool. [*Received, December 1st*, 1926.]

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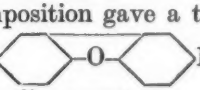
*Reduction Products of Some Nitrodi-*p*-tolyl Ethers.* By Joseph Reilly and Herbert S. Boyd Barrett.

As an extension of previous work (this vol., p. 67) the preparation of 3-nitro-, 3- and 2-amino-di-*p*-tolyl ethers, the partial reduction of the 2 : 6-dinitro-compound, and the nitration of 2-nitrodi-*p*-tolyl ether are now described. The 2-diazonium chloride derivative, $C_6H_4Me{\cdot}O{\cdot}C_6H_3Me{\cdot}N_2Cl$, on decomposition gave a tar-like product from which di-*p*-tolylene ether,  , and chloro-di-*p*-tolyl ether were isolated in small amounts.

3-*Nitrodi*-p-*tolyl ether* was prepared by heating potassium *p*-tolyl-oxide (21 g.) and 4-bromo-2-nitrotoluene (27 g.) with *p*-cresol (40 g.) (solvent) and copper bronze (0·2 g.) at 230—240° for 3 hours. On fractionation of the dried ethereal extract under diminished pressure, the 3-*nitro*-compound was obtained as a pale yellow oil, b. p. 206°/11 mm. (Found : N, 5·8. $C_{14}H_{13}O_3N$ requires N, 5·7%). It is freely soluble in benzene and ether, much less so in cold alcohol, and insoluble in water. Reduction with stannous chloride and hydrochloric acid gave the corresponding amine. The *hydrochloride*

of this was obtained in colourless needles, m. p. 190—195° (Found: Cl, 14·2. $C_{14}H_{15}ON,HCl$ requires Cl, 14·2%). The *base* prepared from the hydrochloride separated from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 76° (Found: N, 6·5. $C_{14}H_{15}ON$ requires N, 6·6%). It is readily soluble in benzene, ether, and acetone, less so in light petroleum, and insoluble in water. The *benzoyl* compound separated from light petroleum in clusters of stout needles, m. p. 107° (Found: N, 4·2. $C_{21}H_{19}O_2N$ requires N, 4·4%). 3-*Aminodi*-p-*tolyl ether chloroaurate* is a bright yellow, crystalline solid (Found: Au, 35·1. $C_{14}H_{15}ON,HAuCl_4$ requires Au, 35·6%). The *azo*-β-*naphthol* compound separated from alcohol in red plates, m. p. 149° (Found: N, 7·8. $C_{24}H_{20}O_2N_2$ requires N, 7·6%).

2-Nitrodi-*p*-tolyl ether was similarly reduced. The 2-*amino*-derivative on fractionation distilled at 196—198°/13 mm. as a colourless oil, which did not solidify at − 15° (Found: N, 6·3. $C_{14}H_{15}ON$ requires N, 6·6%). The *hydrochloride*, colourless blades, m. p. 180—184°, and the *sulphate*, m. p. 160—162°, were prepared. The addition of the 2-diazonium chloride solution to boiling sulphuric acid (50%), followed by distillation in a current of steam, gave a colourless oil which quickly solidified. This solid was separated by fractional crystallisation into two substances of m. p.'s 70° and 165°. The latter substance was identified as a di-*p*-tolylene ether by the method of mixed melting point. The compound, m. p. 70°, appeared to be 2-chlorodi-*p*-tolyl ether.

Partial reduction of 2 : 6-dinitrodi-*p*-tolyl ether between 50° and 60° with stannous chloride gave the 6-*nitro*-2-*amino*-derivative. The *hydrochloride*, m. p. 206—210°, crystallised from ether–alcohol in colourless rosettes. The pure base, m. p. 120—122°, obtained from the hydrochloride, separated from light petroleum (b. p. 80—100°) in light yellow needles. On diazotisation in hydrochloric acid it gave an unstable product. The *azo*-β-*naphthol* compound was obtained as a dark brown, crystalline solid, m. p. 190—200° (Found: N, 10·4. $C_{24}H_{19}O_4N_3$ requires N, 10·2%).

Nitration of 2-nitrodi-*p*-tolyl ether with nitric acid (*d* 1·5) gave mainly 3 : 5-dinitro-*p*-cresol, together with 2 : 2′-dinitrodi-*p*-tolyl ether, m. p. 126°.—University College, Cork. [*Received*, *April* 11*th*, 1927.]